# South African Medical Journal
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# INAUGURAL ADDRESS OF THE PRESIDENT OF THE COLLEGE OF PHYSICIANS AND SURGEONS OF SOUTH AFRICA*

G. A. ELLIOTT, M.D., F.R.C.P.

The applause with which you welcome me tonight is a token of your goodwill not only towards me personally but, what is more important, towards the College of Physicians and Surgeons of South Africa. In those moments of despondency that are bound to be my experience whilst striving to achieve the objects of the College, the echo of this applause will be a source of inspiration, energy and hope towards the completion of our task.

I have in my career undertaken many tasks, but few so responsible and none, as I anticipate, so pleasantly onerous as that for which I was yesterday chosen by my colleagues of the College, the task of being its first President. It is an honoured position, and I appreciate it; but only with the advice and support of all my colleagues, particularly of those who have been elected to its first Council, and with the support of those bodies—so many that it seems like all the world—who have this evening presented greetings and messages of goodwill, will it be possible for me to assist in achieving the objectives of the College. Your goodwill is deeply appreciated.

In expressing my thanks I wish to mention by name only one person—Sir Walter Mercer. As a tangible token of our appreciation of the honour he, as President of the Royal College of Surgeons of Edinburgh, has accorded us by his offices tonight, the Council of the College in a simple ceremony this morning admitted him to Honorary Fellowship of the College.

In thinking, as I must, of the future of this new professional body in South Africa, I cast my mind back into the past to the evolution of those major professional bodies now functioning in South Africa which have contributed and will continue to contribute jointly towards the establishment and maintenance of standards of professional and medical education. Until the founding of the College there were 3 such bodies, the Medical Association of South Africa, the Universities with Medical Faculties, and the South African Medical and Dental Council.

* At the Inaugural Ceremony of the College in the Great Hall of the University of the Witwatersrand, Johannesburg, 8 August 1956.

## FOUR MAJOR PROFESSIONAL BODIES

It seemed to me to be not out of place to choose as the theme of my remarks the evolutionary process which has brought these bodies into existence, and to describe briefly the present and future functions which justify their separate existence.

Oldest of them all, and father of the others, is the *Medical Association of South Africa* (known by several names through all its history), an association of professional men which has always, since its inception, been proudly based upon a voluntary membership, and in whose councils have been sown the seeds that have largely contributed to the genesis of the others.

The first voluntary medical group of which any substantial records exist was founded at the Cape in 1827, and was known as the Cape Medical Society. It was formed primarily to promote professional knowledge, a purpose which it achieved by regular scientific meetings and by establishing a library of books and journals. So keen were the founders to ensure good attendance that one of their self-imposed rules required that all members absent after the chair had been taken for the evening, be fined for their late attendance or non-attendance.

As time passed the functions of the Society extended. Even in those days a tariff of fees was found to be necessary, and in 1830 professional advice at the doctor's house cost 1s.6d., reduction of fractures cost 30s., and for a 'capital' operation (how ominous a description for any operation!) the fee varied from £3 to £15. It cost father a mere £2 for mother to have a baby, in addition, of course, to the usual amount of paternal anxiety traditionally associated with such events.

In the same year (1830), the interest of the Society was still widening, and it addressed itself to the provision

of some form of support for the widows of deceased colleagues. What could be more generous and more touching than their agreement to pledge themselves, the surviving and new members of the Society, to pay to the widow for a period of 12 months after her husband's death all fees derived from medical attention by themselves on families previously attended by the deceased colleague.

*South African Medical and Dental Council.* In 1831 another interesting extension of function occurred, this time at the request of the Colonial Secretary. The Cape Medical Society became the scrutineer of all medical diplomas of those wishing to practise locally, and carried out statutory examinations in Pharmacy. A statutory Medical Committee, which had previously existed but which had been disbanded, was re-formed in 1834 and took over these functions. This statutory Medical Committee later became known as the Medical Board, which was the forerunner of the present South African Medical and Dental Council formed by Act of Parliament in 1929.

*The Medical Schools.* In the 1890s the Society, now known as the Cape of Good Hope (Western Province) Branch of the British Medical Association, through the medium of its President, made requests for what were the beginnings of medical education in South Africa. Thus, in 1895 it was recommended that teaching in botany, zoology, chemistry and physics be instituted at the South African College, of a standard that would be accepted by overseas medical schools. In 1898, the request was extended to the founding of chairs of Anatomy and Physiology; it was noted that the time was not ripe for a full medical curriculum. The war then interfered with htese developments, and it was in 1907 that the President, the late Dr. E. Barnard Fuller, known to many of us, asked that a deputation be received by the Government with a view to the establishment of chairs of Anatomy, Physiology and Pharmacology and, with a vision which he lived to see fulfilled 12 years later, he foresaw 'a full medical faculty in the shadow of Table Mountain'. From these small beginnings in the voluntary body of what is now known as the Medical Association of South Africa have arisen our present Medical Schools, first Cape Town, then Witwatersrand, followed by Pretoria, Durban and Stellenbosch.

*The College of Physicians and Surgeons.* In 1946, within this same voluntary group, arose the concept of the College, a College to be independent in its own right, the inaugural ceremony of which is being celebrated here tonight.

## THEIR FUNCTIONS

We now therefore have 4 major professional bodies in South Africa. What are their common and separate functions, their interrelationships, and their relationships to the public? What is the justification for their separate existence? These were the questions I asked myself when I contemplated taking a share in the development of the College.

As it happens, I am privileged to belong to all four of these bodies—the Medical Association of South Africa, the South African Medical and Dental Council, the University of the Witwatersrand with its Medical Faculty, and now the College. From within each, and from without, I see much purpose common to them all—the setting and maintenance of professional and ethical standards of medical practice, and the right to initiate and recommend measures for the improvement of these standards. This common ground bass, played on the pedals, harmonizes perfectly with the melodies played on the manuals by each body separately, the melodies on the manuals being functions which by Statute, evolution or circumstance have become specialized to each body.

What are the separate functions of each?

The Medical Association of South Africa, the breadth of whose interest through the years I have attempted to describe, by force of circumstance has had to address itself today particularly to conditions of practice, the ethics of practice, and the maintenance of living standards—but this is not to say that it has failed in its function of stimulating the scientific spirit, which it does by its regular scientific congresses.

The South African Medical and Dental Council is a statutory body, its particular functions being the setting of standards of medical education and of the ethics of medical practice, the registration of medical degrees and diplomas, advising the Government on matters of health and medical education, and seeing that the impact of the profession on the public and of the public on the profession is in keeping with the best traditions of public health and welfare.

The Medical Schools have the specialized function of systematic education, undergraduate and postgraduate, and the award of degrees and diplomas to those whom they educate. They are not examining bodies for all and sundry, and to this extent they are, by Statute, 'closed shop', for they cannot by Statute admit to their higher postgraduate examinations those medical practitioners who, for one reason or another, are not able to gain entry as postgraduate students. A most important function of the Medical Schools is to carry out unfettered research, which is the soul of medical and scientific advance and progress. The Schools have the responsible task of stimulating cultural development at the most impressionable age of youth. Those of you who may doubt that this aspect of education is attended to need only inspect the trees in Esselen Street outside the Medical School of the University of the Witwatersrand, on whose trunks are affixed notices advising students of meetings of musical societies, concerts, philosophical societies, religious groups, debating societies, art exhibitions and the like. You *may* even occasionally see notices referring to rugby!

## FUNCTIONS OF THE COLLEGE

And the College? At this early stage of its existence, such views as I may express must obviously be tempered by personal urges and thoughts; we have, however, had opportunity for discussion together during the last few days, and what I say cannot be grossly out of conformity with the generally held views of fellow members of the College.

The broadest function of the College will be to provide

the stimulus and the facilities for professional advancement for medical practitioners whilst they are engaged in practice. Many practitioners, through limitation of posts in the Medical Schools, or for personal reasons, are unable to satisfy their urge to improve their knowledge by gaining access to the Schools as postgraduate students, and are therefore unable to sit the higher examinations provided by the Schools. The College hopes to provide high standard qualifications after examination for such practitioners, which qualifications will, we trust, be accepted for registration by the South African Medical and Dental Council.

The College hopes to sponsor, with the cooperation of the appropriate authorities, facilities for maintaining a high standard of practice, by refresher and other types of course, particularly in the non-teaching hospitals. These courses would be intended for practitioners in active private practice.

The College will sponsor lectureships and prizes. The first prize has already been endowed in terms of a bequest from the late Mr. Lionel Bernard Goldschmidt of Cape Town, who was Chairman of the Steering Committee which preceded the first Council of the College, elected a month ago.

These functions will not intrude upon the functions of Medical Schools or of the Medical Association of South Africa. The College will serve purposes not covered by existing bodies. In this respect it may be claimed that it is doing no more than filling in gaps. But after all, cement only fills in gaps!

I see living space and need for all four of the professional bodies so briefly discussed, each with ideals common to the others, and each with functions specific to itself.

The main objectives of the College are clear. Their achievement will be attained by the enthusiasm of its members, and with the cooperation and understanding of its 3 elder brethren—the Medical Association of South Africa, the South African Medical and Dental Council, and the Universities with Medical Schools. We must hasten slowly, step by step. We shall meet difficulties, but nothing that was ever worth while was achieved easily or quickly.

I conclude on a note of cooperation by quoting the 17th-century philosopher Spinoza, a Spaniard, whose country of adoption was Holland after his expulsion from Spain under the Inquisition, but who nevertheless remained unembittered, and who tried to show that it is possible to live nobly even when we recognize the limitations of human potential and the limitations of human nature. He wrote: 'Let us join hands and help, for today we are alive together'.

## OFFICIAL ANNOUNCEMENT : AMPTELIKE AANKONDIGING

### NOTICE OF MOTION

Minute 80 of the record of the last meeting of the Federal Council contains the following resolution:

'That the policy of this Association shall be to ensure a free choice of doctor by the patient and of patient by the doctor. In pursuance of this policy all future appointments to Benefit Societies should be on the basis of open panels for general practitioners and specialists, unless in exceptional circumstances and after approval by Federal Council.'

Notice of motion has been given at the forthcoming meeting of the Federal Council to review this resolution, over the names of Dr. A. L. Agranat and Dr. E. W. Turton. The notice of motion is published for general information and reads as follows:

'In view of the considerable difficulties and embarrassment and probable unfavourable repercussions caused by an attempt to implement the resolution of Federal Council on the question of an open panel for all Benefit Societies, adopted at its meeting in April 1956, we move that the resolution be rescinded and that Federal Council appoint a Committee to investigate and report on the practicability and advisability of applying the open panel system to Benefit Societies.'

A. H. Tonkin
*Secretary*

Medical House
Cape Town
10 August 1956

### KENNIS VAN VOORSTEL

Die volgende besluit verskyn in notule 80 van die verrigtinge van die jongste vergadering van die Federale Raad:

'That the policy of this Association shall be to ensure a free choice of doctor by the patient and of patient by the doctor. In pursuance of this policy all future appointments to Benefit Societies should be on the basis of open panels for general practitioners and specialists, unless in exceptional circumstances and after approval by Federal Council.'

Kennis van voorstel om hierdie besluit by die eerskomende vergadering van die Federale Raad in hersiening te neem is deur dr. A. L. Agranat en dr. E. W. Turton gegee. Die kennis van voorstel word vir algemene inligting gepubliseer en lui as volg:

'In view of the considerable difficulties and embarrassment and probable unfavourable repercussions caused by an attempt to implement the resolution of Federal Council on the question of an open panel for all Benefit Societies, adopted at its meeting in April 1956, we move that the resolution be rescinded and that Federal Council appoint a Committee to investigate and report on the practicability and advisability of applying the open panel system to Benefit Societies.'

A. H. Tonkin
*Sekretaris*

Mediese Huis
Kaapstad
10 Augustus 1956

## RESEARCH FORUM

*Research Forum*, Department of Medicine, University of Cape Town. Two meetings of the Research Forum will be held during September, both at 12 noon in the large A-floor lecture theatre, Groote Schuur Hospital, Cape Town.

1. *Tuesday*, 4 September 1956. Subject, *Porphyria*. Speakers: Dr. L. Eales—*Clinical Experiences with porphyria*, Dr. S. Saunders —*Rapid test for identification of stool porphyrins*. Dr. E. Dowdle (in collaboration with Prof. G. C. Tinder—*A Cape Coloured family with porphyria*.

2. *Tuesday*, 11 *September* 1956. Subject, *The Diagnosis of Pernicious Anaemia*. *Speaker*, Dr. E. Davidson.

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## EDITORIAL

### THE VIRGIN BIRTHS NEWSPAPER FEATURE

As the *Lancet*[1] remarks, no 'reasonable man' would even entertain the possibility that a woman might become pregnant without a single spermatozoon entering her uterus. For centuries scientists would have agreed with this view, but biologists today are not quite so certain.

Dr. Helen Spurway, lecturer in Biometry and Eugenics in London, set the cat among the pigeons by some remarks about possibilities in mammals, and even man, in a lecture she recently gave entitled 'Virgin Births' concerning her observations on the guppy (*Lebistes reticulatus*), a small live-bearing fish. Apparently the female fish may be kept separate from all males from birth and yet give rise to broods, which consist almost entirely of females (1 male and 1 intersex were reported among 92 such offspring). There are 3 possible explanations for this unusual finding in a vertebrate animal. First, the possibility that the mother-fish might have been fertilized by paternal sperm while she was still an embryo *in utero* can be excluded on genetic grounds. Secondly, hermaphroditism, in which ova and sperm arise from the same organism and self-fertilization occurs, is known to be possible in fishes. The third possibility is parthenogenesis, a phenomenon which occurs normally in certain insects, for example. In parthenogenesis the ovum starts to divide without being fertilized, so producing offspring with half the usual number of nuclear chromosomes, unless some sort of doubling-up occurs. In any event, the progeny of such procreation can never show genetic features which are not found in the mother. On the other hand, since the offspring will inherit only half of the maternal chromosomes, there will always be features in the mother which the children will not possess.

From Dr. Spurway's work there seems little doubt that parthenogenesis can occur in the guppy, despite the fact that in warm-blooded vertebrate animals it is certainly very uncommon. Parthenogenetic division of the ovum has been found in the cat and the ferret, but the embryos were not viable. Healthy offspring have,

## VAN DIE REDAKSIE

### KOERANT-OPHEF OOR MAAGDELIKE GEBOORTES

Soos die *Lancet*[1] dit stel, sal geen ‚verstandige man' ooit eers die moontlikheid oorweeg nie dat 'n vrou swanger kan raak sonder dat 'n enkele saadsel haar baarmoeder binnegaan. Vir eeue sou wetenskaplikes met hierdie mening saamgestem het, maar bioloë is vandag nie meer heeltemal so seker van die saak nie.

In haar lesing getiteld ‚Virgin Births' oor haar waarnemings i.v.m. die guppy (*Lebistes reticulatis*), 'n klein eierlewendbarende vis, het dr. Helen Spurway, Lektrise in Biometrie en Eugenetiek in Londen, onlangs, figuurlik gesproke, die kat tussen die duiwe gelos deur 'n paar van haar opmerkings oor die moontlikheid van maagdelike geboortes by soogdiere en selfs by die mens. Blykbaar kan die wyfievis van geboorte heeltemal van alle manatjievisse afgesonder word en tog 'n groot broeisel wat feitlik net uit wyfievisse bestaan, voortbring—(een manlike en een interseksuele geval onder 92 van sulke afstammelinge is aangemeld). Daar is drie moontlike verklarings vir hierdie ongewone bevinding by werweldiere. Eerstens kan die moontlikheid dat die moedervis deur 'n vaderlike saad bevrug is terwyl sy nog *in utero* 'n embrio was, op genetiese gronde, uitgeskakel word. Tweedens is dit bekend dat dubbelslagtigheid (waar eiers en saad van dieselfde organisme ontstaan en self-bevrugting plaasvind), by visse aangetref word. Die derde moontlikheid is partenogenese, 'n verskynsel wat gewoonweg, by sekere insekte byvoorbeeld, voorkom. In so 'n geval begin die eiersel verdeel sonder dat dit bevrug is, en produseer vervolgens 'n afstammeling met slegs die helfte van die gewone aantal kernchromosome, tensy daar een of ander mate van verdubbeling plaasgevind het. Die nakomelinge van so 'n voortteling kan in elk geval nooit enige genetiese faktore wys wat nie in die moeder aangetref word nie. Aan die ander kant, aangesien die nakomelinge slegs die helfte van die moeder se chromosome sal erf, sal daar altyd sekere kenmerke in die moeder wees wat nie in die kinders aangetref sal word nie.

Volgens dr. Spurway se werk is daar min twyfel dat partenogenese wel in die guppy voorkom, ten spyte van

however, been induced in rabbits without mating by cooling the fallopian tubes.[2]

In view of this Dr. Spurway went on to consider the likelihood of spontaneous parthenogenesis in mammals, including man. Even if it did occur it would be very difficult to recognize, and the animals concerned would have to be observed under the most stringent conditions of isolation. It may be assumed that, if fatherless offspring were produced at all in mammals, it would be through the mechanism of parthenogenesis rather than hermaphroditism.

In man parthenogenesis would also be difficult to recognize and to prove. It could never be even suspected in women in whom intercourse had recently taken place. That it is very rare (to say the least) can be deduced from the absence of any known report of fatherless pregnancy emanating from women's prisons or other places of total female segregation.

Present-day biological knowledge would make it possible to disprove almost all false claimants to fatherless offspring, but even today it is doubtful whether a true candidate could be vindicated with certainty. The parthenogenetic offspring would be a female (just possibly an abnormal male), closely resembling her mother in physical characteristics. Blood grouping, including use of the rare types, together with a few other known hereditary features, such as eye colour (if definite) and ability to taste phenyl thio-urea, would eliminate the great majority. The final test would be the ability of a skin graft derived from the child to take in the mother and persist indefinitely without breakdown. (A skin graft the other way round would not persist because the mother would probably possess antigens which the child did not.) The interpretation of skin-grafting results, however, does not yet seem to be entirely agreed upon by cytogeneticists, although Dr. Spurway apparently considers that they would be conclusive one way or the other.

The British *Sunday Pictorial*[3] took over at this point and initiated an enquiry, asking any mother who believed she had produced a parthenogenetic infant to come forward. Nineteen pairs of mothers and daughters did so. Eleven were immediately eliminated because they thought that an intact hymen must indicate a virgin birth. Of the remaining 8, 6 were eliminated by blood grouping and one by eye colour. The one pair who passed these tests were also alike in ability to taste phenyl thio-urea, in A-substance secretor tests, and in serum-protein electrophoretic pattern. Despite these similarities, however, a skin graft from daughter to mother was shed in approximately 4 weeks. Thus

die feit dat dit in warmbloedige werweldiere sekerlik baie seldsaam is. Partenogenetiese verdeling van die eiersel is in die kat en die muishond aangetref, maar die embrios was nie lewensvatbaar nie. Deur die eileiers[2] te verkoel, is gesonde afstammelinge van hase, sonder paring, voortgebring.

Met die oog hierop het dr. Spurway verder die moontlikheid van spontane partenogenese in soogdiere, insluitende die mens, oorweeg. Selfs al sou dit gebeur, sou dit baie moeilik wees om dit te herken en die betrokke diere sou onder die strengste omstandighede van afsondering waargeneem moet word. Dit mag aangeneem word dat as vaderlose afstammelinge enigsins in soogdiere voortgebring sou word, dit deur die meganisme van partenogenese, eerder as deur dubbelslagtigheid, sou geskied.

Dit sou ook moeilik wees om partenogenese in die mens te herken en te bewys. Die gedagte daaraan kan nooit eers gekoester word nie in vroue waar gemeenskap kort vantevore plaasgevind het nie. Dat dit uiters seldsaam is (om die minste te sê), kan afgelei word van die feit dat geen kennis gedra word nie van enige verslag van vaderlose swangerskap wat in tronke vir vrouens of ander plekke van algehele vroulike segegrasie voorgekom het.

Hedendaagse biologiese kennis maak dit moontlik om feitlik alle valse aanspraakmakers op vaderlose nakomelinge, te weerlê; maar dit is selfs vandag nog twyfelagtig of die aanspraak van 'n ware kandidaat met sekerheid gestaaf kan word. Die partenogenetiese afstammeling sal vroulik wees (dit mag net moontlik 'n abnormale manlike afstammeling wees) wat, sovêr dit fisiese karaktertrekke betref, baie na haar moeder sal aard. Die grootste meerderheid sal deur bloedgroepering, insluitende die gebruik van die seldsame tipes, tesame met 'n paar ander bekende oorerflike kenmerke, soos die kleur van die oë (as dit duidelik is) en die vermoë om feniel tio-urea te proe, uitgeskakel word. Die finale toets is as 'n veloorplanting wat van die kind verkry is op die moeder vat en vir 'n bepaalde tyd sonder instorting volhou. ('n Veloorplanting van die moeder op die kind sal nie hou nie, aangesien die moeder moontlik antigene sal besit wat die kind nie sal hê nie). Dit lyk egter of sitogenetici nog nie heeltemal ooreenstem met die interpretasie van die resultate van veloorplanting nie, alhoewel dr. Spurway oënskynlik reken dat dit afdoende bewys daarvoor of daarteen lewer.

Op hierdie stadium het die *Sunday Pictorial*[3] oorgeneem en 'n ondersoek op tou gesit, waarin hulle gevra het dat enige moeder wat glo dat sy 'n partenogenetiese baba in die wêreld gebring het, haarself moet aanbied. Neëntien pare moeders en dogters het hierop gereageeer. Elf is onmiddellik uitgeskakel, aangesien hulle gedink het dat 'n ongeskonde maagdevlies 'n maagdelike geboorte moet aandui. Van die oorblywende ag, is ses deur bloedgroepering en een deur die kleur van die oë uitgeskakel. Die een paar wat in hierdie toetse geslaag het, was eenders in hulle vermoë om feniel tio-urea te proe, en in afskeiertoetse vir A-stof en in serum-proteïen-elektroforesiese patroon. Afgesien van hierdie ooreenkoms egter, is 'n veloorplanting van die dogter op die moeder in ongeveer 4 weke afgewerp.

it seems that this mother's claim cannot be upheld, and we must still look for further evidence of human parthenogenesis.

1. Editorial (1955): Lancet, **2**, 967.
2. Pincus, G. and Shapiro, H. (1939): Proc. Nat. Acad. Sci., **26**, 163.
3. Balfour-Lynn, S. (1956): Lancet, **1**, 1072.

Dit lyk dus of hierdie moeder se eis nie gestaaf kan word nie en ons moet nog steeds soek na verdere bewyse van menslike partenogenese.

1. Van die Redaksie (1955): Lancet, **2**, 967.
2. Pincus, G. en Shapiro, H. (1939): Proc. Nat. Acad. Sci., **26**, 163.
3. Balfour-Lynn, S. (1956): Lancet, **1**, 1072.

# THE MEDICAL AND PUBLIC HEALTH IMPORTANCE OF THE COXSACKIE VIRUSES

JAMES GEAR, V.MEASROCH AND F. R. PRINSLOO

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The Coxsackie group of viruses derived their name from the Hudson River Town, Coxsackie, in New York State, where the first two members of this group were identified by Dalldorf and Sickles in 1947.[1] Both these viruses were isolated in suckling mice from the faeces of children acutely ill with paralytic poliomyelitis. The pathogenicity for suckling mice is one of the distinguishing features of this group of viruses, and their relative lack of pathogenicity for adult mice and other experimental animals accounts for their escape from recognition hitherto.

Subsequent studies have shown that there are 2 groups of Coxsackie virus, named groups A and B. Mice infected with group-A strains develop flaccid paralysis and on histological examination show only hyalin degeneration and active repair of the voluntary striated muscles. This diffuse muscle destruction and the absence of lesions elsewhere are characteristic of group-A strains. Mice infected with group-B strains develop weakness, tremors, spasms, and paralysis. The voluntary muscles show focal lesions. The pads of fat between the scapulae show whitish degeneration and on microscopic examination necrosis and an inflammatory reaction, followed later by calcium deposits in the necrotic areas. This lesion of the fat pad is unique and characteristic of Coxsackie-B virus infection. The central nervous system is often involved, showing a patchy dissolution of the parenchymal cells and associated with an inflammatory infiltration, particularly in the region of the blood vessels. The heart muscle may also show foci of necrosis and acute inflammation. Similar focal lesions may be found in the pancreas and liver. These histological pictures are of differential value in distinguishing Coxsackie group-A viruses from Coxsackie group-B viruses. Serological studies have revealed that there are at least 17 different immunological types of group-A virus and 5 of group-B virus.

When they were discovered and for some time afterwards it was not known what diseases the Coxsackie viruses caused. The cases from which the first two viruses were isolated were proved to be true cases of paralytic poliomyelitis infected also with poliovirus. As a result of more recent studies their pathogenicity has now been more clearly defined.[2] The group-A viruses have been incriminated as the cause of herpangina and, as the present studies show, are possibly related to a number of other illnesses. Coxsackie-B viruses have been incriminated as the cause of Bornholm disease and, as the present studies show, in parts of Southern Africa are important causes of aseptic meningoencephalitis and of myocarditis neonatorum. A study to assess the importance of these viruses in South Africa was begun about 5 years ago and this paper besides giving more general information based on the observations of others in other countries summarizes our findings in Southern Africa.

## *Incidence of Coxsackie Virus Infections*

An epidemiological study of a group of Bantu (African) infants, living under slum conditions in an urban Native township, was undertaken to determine the incidence of these infections. This study has now extended over 4 years and the results will be described in detail in another paper. At present it is of interest to note that during this period most of the then known types of Coxsackie virus were isolated and identified. In addition several new types, confirmed as such by Dalldorf and Sickles, were brought to light. Unfortunately, it was not always possible to relate these infections to illness. However, other studies proceeding concurrently have defined the clinical conditions caused by these viruses. Both groups are of importance and will be considered separately.

### COXSACKIE GROUP-A VIRUS INFECTIONS

### *Herpangina*

Herpangina was first described in 1920 by Zahorsky.[3] More recently studies by Huebner[4] and others have shown that this condition is caused by Coxsackie group-A viruses. The patients are taken suddenly ill, often with high fever, at times accompanied by chilliness, fatigue,

nausea, anorexia, vomiting, and abdominal pain, and occasionally diarrhoea. They suffer from headache, pain in the neck, back and extremities, and muscle tenderness. They experience moderate pain on swallowing, but do not have respiratory symptoms. Papulovesicles, about 2-10 in number, are found in the posterior part of the mouth, varying in size from a grain of rice to a pea, often arranged in groups and surrounded by a marked reddened area. The lesions are confined to the soft palate, the uvula, and the anterior and posterior parts of the fauces, and they also occur in the posterior wall of the pharynx and the tonsils and are often associated with intense congestion of the fauces and tonsils. The vesicles often rupture to form superficial ulcers, covered with a thin greyish-white exudate. The illness is benign and the temperature returns to normal within 2-4 days after onset. The disease exhibits a seasonal peak during the summer and autumn months. It is common in South Africa, and Coxsackie-A virus has been isolated from cases in several outbreaks, thus confirming its aetiological role.

*Acute Febrile Lymphadenitis*

An outbreak of an illness clinically resembling glandular fever, affecting many of the residents of a school hostel in Middelburg, Transvaal, was studied in collaboration with Dr. I. M. Patz. This outbreak will be described in detail in a separate paper. At present it suffices to note that of 200 children from 5 to 13 years of age in this primary school hostel, 30 were affected in 3 distinct waves during the period from 8 August to 16 October 1953. These patients at the onset, which was sudden, complained of feeling feverish and of enlarged tender glands, sometimes associated with painful stiffness of the neck. The temperature ranged from 99°F to 103·4°F and in the majority of cases lasted from 24 to 96 hours, with a range from a few hours to 10 days. The majority of patients also complained of frontal headache. Only 20% complained of sore throat, particularly on swallowing. Blisters suggestive of herpangina were not seen and there was no membrane apparent. The fauces were slightly injected. Abdominal pain occurred in 2 cases and vomiting in 3. In 28 of these 30 cases lymphadenopathy was found, involving the cervical glands. In most cases more than one group of glands were involved, often successively. The glands were painful and tender. The axillary and inguinal glands were involved in only 2 of the cases. Enlargement of the spleen was detected in 3 of the patients. No rash was seen in these cases, but in some patients with a similar condition in Johannesburg at the same time a few roseolar spots, somewhat like the rose spots of typhoid fever, were seen on the abdomen. Relapses after an interval of 4 days and 6 weeks respectively occurred in 2 cases. The majority of patients made a good recovery. The Paul-Bunnell test gave negative results in 24 of the 25 children whose blood was taken for this test. The remaining case gave a titre of 1 : 160, suggestive of glandular fever, but unfortunately absorption tests were not done. However, it is clear from these findings that these cases in their serological tests did not conform with classical glandular fever. This opinion was supported by the results of the blood count made on 23 of these cases on the 3-4th day of illness and 1 week and 3-4 weeks later. The leucocyte count varied from 5,200 to 17,300 and the majority of cases (15 of 23) had initial counts of over 10,000 white cells per c.cm. with a neutrophilia. In none of the cases was the blood picture suggestive of glandular fever.

Coxsackie group-A virus was isolated from the stool of 5 of these patients and from the blood of one of them. These 6 viruses were typed and, somewhat unexpectedly, 3 were found to be Type-5 and 3 to be Type-6 Coxsackie-A viruses. The finding of the virus in the stool of a patient does not necessarily mean that it is responsible for the patient's illness. However, the suspicion that this condition was caused by Coxsackie-A virus is greatly strengthened by finding this virus in the blood of one of the patients.

*Meningo-encephalitis*

In a study of cases of meningo-encephalitis admitted to the Johannesburg Fever Hospital in the summer and autumn of 1953-54, it was noted that a Coxsackie group-A virus was isolated from the faeces of 5. It was pointed out then that this may have been a coincidental finding. However, from 3 of these 9 cases the same type of virus was also isolated from the cerebrospinal fluid. It therefore was clear that, in these 3 cases at least, the illness was caused by Coxsackie-A virus.

Since that time several similar cases have been investigated. These were admitted to hospital with a provisional diagnosis of poliomyelitis. Several of these patients were less than 2 years of age, but those old enough to complain said that their illness had a fairly sudden onset, with sore throat, slight nausea, and sometimes vomiting, muscle pain and headache. After they had been feverish for 2-3 days their headache became severe and painful stiffness of the neck and back developed. None developed paralysis.

Lumbar puncture revealed a clear fluid, but on microscopical examination a pleocytosis with a variable proportion of polymorphonuclear cells and monocytes was noted. The routine tests for the presence of poliovirus in the faeces gave negative results. However, in 7 such cases Coxsackie group-A virus was isolated from the faeces in 3, from a throat swab in one, and from the cerebrospinal fluid in 3. These latter findings clearly indicate that the meningo-encephalitis of these patients was due to Coxsackie group-A virus.

This conclusion is supported by Johnsson and Lindahl[6] who, in a study of herpangina occurring in Stockholm, Sweden, noted that one of their cases presented signs of encephalitis and another the signs of aseptic meningitis. From both these cases Coxsackie group-A virus was isolated from the faeces. There thus is little doubt that Coxsackie group-A virus is a cause of meningo-encephalitis.

*Association with Poliovirus in cases of Paralytic Poliomyelitis*

It will be recalled that the first two Coxsackie viruses identified were isolated from cases of paralytic polio-

myelitis, from which poliovirus was also isolated. It is now clear that this association frequently occurs in cases of paralytic poliomyelitis. It has been suggested that it is purely coincidental, and it may well be. However, Coxsackie group-B viruses are rarely found in association with poliovirus.

In our studies carried out since 1953, of 80 cases from which Coxsackie group-A virus was isolated poliovirus was also isolated from 27; i.e., in 1/3rd of the cases found to be infected with Coxsackie virus there was also an infection with poliovirus. Conversely, from 25% of the cases proved to have poliomyelitis by the isolation of poliovirus, Coxsackie group-A virus was also isolated. There is thus no doubt that these two viruses frequently occur in association. Some patients with paralytic poliomyelitis have also been found to have lesions resembling herpangina in their throats, presumably due to the coincident Coxsackie-A virus infection. It seems possible that Coxsackie-A virus and poliovirus may have a synergic action in some cases of paralytic poliomyelitis. This possibility certainly merits further study to define the relationship between these two viruses in such cases.

*Guillain-Barré Syndrome*

Clinically this syndrome manifests itself as a symmetrical weakness or paralysis, often associated with paraesthesias. It is the condition most often confused with poliomyelitis. Pathologically it is characterized by changes in the nerve roots consisting of cellular infiltration and fragmentation of the myelin sheaths. The obstruction to the flow of cerebrospinal fluid at the nerve roots probably accounts for the increase in protein content without a corresponding increase in the cell count of the cerebrospinal fluid, the characteristic clinico-pathological finding. Many cases occur as post-infective complications of the acute specific fevers and within the last 2 years 2 cases following chicken-pox and one following Q fever have been seen in the Johannesburg Fever Hospital. Other cases appear to be related to an auto-allergic reaction to drugs, particularly the sulpha drugs. Some cases appear to be the result of infection. It is apparent then that the aetiology of the syndrome remains uncertain. It is therefore of interest to note that in a consecutive series of 7 cases studied in these laboratories Coxsackie group-A virus was isolated from the faeces of 4. It is possible therefore that in these cases there was an aetiological relationship. It is our belief that most cases of this syndrome are not related to Coxsackie-A virus infections and have some other basis. On the other hand some cases may result from infection of the cells of the supporting tissue with Coxsackie-A virus. Further study is necessary to define the significance of the finding of this virus in these cases.

*Bell's Palsy*

During the 3-year period of this study, Coxsackie group-A viruses were isolated from the faeces of 2 cases, and the throat swab of another case, of Bell's palsy. Again it is possible that the virus had a causal relationship to the patients' illness, but further study will be necessary to prove this.

*Miscellaneous Conditions*

Coxsackie group-A viruses were isolated from the faeces of a number of cases clinically diagnosed as myositis. One of these patients, a boy 15 years old, had a febrile illness lasting several weeks and was clinically diagnosed as a case of dermatomyositis. He was treated with cortisone for some weeks. It seemed possible that this treatment aggravated and prolonged his illness, but he eventually recovered completely.

*Summer Diarrhoea*

Coxsackie group-A viruses have been isolated from a number of cases of summer diarrhoea in infants. Again it is possible that there is a causal relationship, but this too awaits proof.

It is apparent that where infections are as prevalent as the Coxsackie-A virus infections it is often difficult to define the significance of these findings. However, they are placed on record, and as further studies are undertaken it will be possible to define their significance more accurately.

## COXSACKIE GROUP-B VIRUS INFECTIONS

Five serological types of Coxsackie group-B virus have been identified. Four of these 5 have been shown to occur in Southern Africa. It is of interest to note that so far Coxsackie group-B Type-1 virus, which appears to be prevalent in the United States, has not been isolated in Southern Africa.

*Bornholm Disease*

The Coxsackie group-B viruses have been incriminated as the cause of epidemic myalgia, Bamle disease or Bornholm disease. In Southern Africa Coxsackie group-B viruses have been isolated from outbreaks of Bornholm disease in Middelburg, Transvaal,[7] in Johannesburg, in Salisbury, and in Bulawayo. This clinical syndrome was first observed in 1856 in Iceland by Finsen, who called it pleurodynia. Since then epidemics have been recognized in all parts of the world. Many of them have been recorded in Scandinavia. In a classical monograph[8] on the subject Sylvest gave this condition the name Bornholm disease after the Danish island Bornholm in the Baltic. The same disease has been called by various other names, some based on the geographical site of its occurrence, such as Skien disease, Bamle disease, Drangedal disease, and others based on the most prominent clinical symptoms, such as epidemic diaphragmatic spasm, epidemic benign pleurisy, and devil's grip.

The disease occurs in epidemic form usually in the summer and autumn. The incidence of infection is usually greatest in children and young adults. The incubation period is 2-4 days. The onset is sudden, usually with pain in the region of the diaphragm, which may be very severe and associated with protective splinting of the lower chest and upper abdomen. It is aggravated by coughing, sneezing, laughing and even breathing. Pain and tenderness of the muscles of the trunk and limbs may also occur. The patient develops fever, a rapid pulse, generalized aches and frontal headache. The condition is characterized by fever, which shows a tendency to one or more relapses,

during which the patient complains typically of severe pain in the lower part of the thorax and epigastrium, but it may occur elsewhere too. In children abdominal pain, nausea and vomiting and occasionally diarrhoea are more frequently seen than the lower thoracic pain. In the relapses the original symptoms recur in most cases with equal severity. Abdominal pain may be so severe that an acute abdominal emergency is suspected, but as a rule marked rigidity of the muscles is not found. In patients with severe chest pain, pleuritic in character, pleural friction rubs may be heard.

*Meningo-encephalitis*

Bornholm disease may be complicated by the development of meningo-encephalitis. Studies recently carried out in the Laboratories of the Poliomyelitis Research Foundation have shown that Coxsackie group-B virus is the commonest cause of meningo-encephalitis in this region.[5] Similar cases occurring in Rhodesia have also been found to be associated with Coxsackie group-B virus infection.[9] Most of these cases were admitted to hospital with a provisional and quite justifiable diagnosis of non-paralytic poliomyelitis. Many of them gave no previous history suggestive of Bornholm disease, but in a number the signs and symptoms of this disease preceded the development of meningo-encephalitis. Most patients gave a history of sore throat, many had abdominal pain, and some had nausea and vomiting. These initial symptoms were often followed by a remission lasting 1-7 days and then the patient again developed fever associated with severe headache, stiff neck and back, and often anorexia, nausea, and vomiting. On admission to hospital the patients had fever and complained of severe headache, stiff neck and back, and pains in the limbs; occasionally they also complained of weakness affecting one or other limb. On examination the outstanding signs were stiff neck and back and slight enlargement of the lymph glands. Most had normal reflexes, but in a few the reflexes were diminished or were unequal on the two sides.

The blood count varied considerably. It was of value in diagnosis in that the very high white-cell counts with a very high neutrophilia, such as occur in the case of bacterial meningitis, were not seen. The examination of the cerebrospinal fluid was of crucial value. Most cases had less than 100 cells. High counts of over 500 cells per c.mm. were not found. In the first lumbar puncture neutrophil leucocytes and lymphocytes occurred in about equal proportions. In the second lumbar puncture done about 2 weeks after the first it was still abnormal in over 60% of the cases, but now there were more lymphocytes than leucocytes. In the diagnosis of this form of meningo-encephalitis various other forms, including bacterial meningitis, fungal meningitis, protozoal infection such as toxoplasmosis and malaria, have to be considered and excluded.

Several other viruses known to cause meningo-encephalitis have also to be considered in the differential diagnosis. Meningo-encephalitis due to the mumps virus may occur either before or after the typical parotitis or orchitis, and many cases are seen without either parotitis or orchitis. The nervous forms of glandular fever often resemble meningo-encephalitis due to Coxsackie group-B virus. The diagnosis can only be established with certainty by the isolation of the virus. In most cases it is isolated from specimens of faeces. In a study carried out on the cases admitted to the Johannesburg Fever Hospital, Coxsackie group-B virus was isolated from the faeces of 20 cases, and from 9 of these 20 the same type of virus was also isolated from the cerebrospinal fluid. There is thus no doubt about the aetiological relationship of these viruses to these cases of meningo-encephalitis. Indeed, Coxsackie group-B virus emerged as the most frequently identified cause of meningo-encephalitis in this region.

*Myocarditis Neonatorum*

In October 1952 an outbreak of an acute fulminating illness occurred in a maternity home in Johannesburg.[10] Of 10 babies affected 6 died after an acute febrile illness ending in circulatory collapse. Post-mortems carried out on 3 of them revealed that the cause of death was acute heart-failure resulting from a focal but extensive myocarditis. In one case a focus of inflammation in the brain and of one suprarenal gland was found, suggesting that the myocarditis was a part of a generalized infection.

Coxsackie group-B virus was isolated from the faeces of 2 of the 4 patients who recovered. Baby mice inoculated with a suspension prepared from the brain and the heart of 2 of the fatal cases showed lesions of the fat pad and brain similar to those caused by Coxsackie group-B virus.

A similar outbreak affecting 3 babies soon after birth in a maternity home in Umtali, Southern Rhodesia, occurred in the autumn of 1954.[11] One of these babies died on the 12th day after birth. The other two recovered after being ill for about 1 week. Microscopic examination of the organs in the fatal case showed congestion but no other pathological change in the brain. The heart, which macroscopically had not appeared grossly abnormal, on microscopic examination revealed scattered foci of inflammation in the substance of the muscle. The muscle showed degeneration and fragmentation associated with a surrounding inflammatory-cell infiltrate mostly of mononuclear cells, histiocytes and lymphocytes, but also including polymorphonuclear leucocytes. The suprarenal showed marked congestion of the medulla, in which a few foci of inflammatory cells were also detected. Viruses resistant to the action of ether and pathogenic to baby mice were isolated from the faeces and caecal contents of the baby who died and from the faeces of one of the babies who recovered. These viruses were successively established on passage in baby mice. Microscopic examination of their tissues revealed an acute necrosis and inflammation of the fat pad. In a proportion of these mice, lesions of the brain and focal necrosis and inflammation of the heart muscle and voluntary muscles were also detected. These lesions resemble those produced by Coxsackie group-B virus. Cross-immunity tests carried out with sera prepared against Dalldorf's

classical strains revealed that this virus was a Coxsackie group-B Type-4 virus. More recently, from the heart of a baby who was admitted to the Transvaal Memorial Hospital for Children 9 days after birth, and who died shortly after admission, a Coxsackie group-B virus has been isolated. This virus has also been typed and found to be a group-B Type-2 virus. The isolation and identification of the virus from the heart of this case provides the final proof that this condition of myocarditis neonatorum is caused by Coxsackie group-B virus. Unlike the other manifestations of Coxsackie group-B infection, this condition is serious and a large proportion of the babies affected may die.

## LABORATORY DIAGNOSIS

Both Coxsackie group-A and group-B viruses are found in the throat and the faeces of cases of the above-described conditions. In many they also occur in the blood stream but, as in most virus diseases, their occurrence there is of short duration. In some cases they occur in the cerebrospinal fluid. They may be detected in the faeces for several weeks.

For the laboratory investigation of these infections and for laboratory confirmation of a clinical diagnosis, the following specimens should be sent to the virus laboratory:

1. *Acute phase*
   (i) Blood with no preservative or anticoagulant
   (ii) Faeces
   (iii) Throat swab
   (iv) CSF (if meningo-encephalitis is suspected and a lumbar puncture is done)
2. *Convalescent phase*
   (i) Blood specimen for antibody titration in comparison with the acute-phase blood

In the laboratory, after appropriate preparation and purification, samples of the acute-phase specimens are inoculated into litters of 1-day-old baby mice and into tissue-culture tubes of human or monkey cells. The mice are observed for 2 weeks for signs of illness, especially for tremors, weakness and paralysis. If any develop the mice are killed with ether. Portions of their organs are fixed in Bouin's solution prior to the preparation of histological sections. Half the brain and the carcase, after the viscera have been removed, are kept and prepared for passage. It is often necessary to passage a suspected isolate 2-3 times before the characteristic clinical and pathological picture is found.

The identification of a virus as belonging to the Coxsackie group depends first on finding the characteristic histological lesions in baby mice. It will be recalled that with Coxsackie group-A viruses this is a diffuse acute myositis characterized by hyalin eosinophil degeneration of the voluntary muscle fibres, with which is associated an acute inflammatory and repair reaction. With Coxsackie-B viruses, only a focal myositis is found and it is not always apparent. The characteristic finding is an acute necrosis of the interscapular fat pad, associated with an acute inflammatory infiltration.

The final identification and typing of the virus is achieved in a serum-neutralization test in which the virus is tested against specific antisera of each of the known types of the corresponding group of Coxsackie virus.

## CONCLUSION AND SUMMARY

From this survey it is apparent that the Coxsackie viruses are important pathogens of Man. They are very prevalent, particularly the group-A viruses and give rise to specific illnesses as well as to some conditions which may simulate other infections.

Coxsackie group-A viruses are the cause of herpangina and are one of the causes of meningo-encephalitis, and of a pyrexial illness of relatively short duration. Evidence has also been obtained suggesting that they may cause an illness clinically resembling glandular fever, but not associated with the characteristic blood picture of that condition and giving a negative result in the Paul-Bunnell test.

Some cases of the Guillain-Barré syndrome have been found to be associated with Coxsackie group-A virus infection. The significance of this association has not been determined, but it is believed that most cases of this syndrome have some other basis.

The relationship of Coxsackie group-A infections to summer diarrhoea and enteritis in infants has also still to be assessed, although these viruses have frequently been isolated from patients with these conditions.

Coxsackie group-A virus is found so often in association with poliovirus in cases of paralytic poliomyelitis that it is suspected that there may be a synergic action of these two viruses in such cases.

Coxsackie group-B viruses cause Bornholm disease and in Southern Africa are the commonest identified cause of meningo-encephalitis. They have also been incriminated in the present series of studies as the cause of outbreaks of myocarditis neonatorum, a serious condition which may end fatally.

An accurate specific diagnosis of these diseases is important from the medical and more particularly from the public-health point of view. This can now be achieved with a considerable degree of certainty in a properly equipped virus-laboratory.

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# 5-HYDROXYTRYPTAMINE

## A REVIEW

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This amine was first detected as 'enteramine' by Vialli and Erspamer in 1933 (Erspamer, 1954) and was then assumed to originate in the argentaffin or Kultschitzky cells of the gastro-intestinal tract. The substance was later isolated from blood, as 'serotonin' (Rapport *et al.*, 1948).

The argentaffin or enterochromaffin cells of the gastro-intestinal mucosa are believed normally to constitute a 'diffuse endocrine gland' and to manufacture the amine 5-hydroxytryptamine (5HT) from the amino acid tryptophan. The 5HT is liberated into the blood and the lymph. It appears to be absorbed, stored and released by the platelets, like certain other vaso-active substances, namely histamine, adrenaline, and noradrenaline.

5HT was produced synthetically as 5HT creatinine sulphate by Hamlin and Fischer (1951).

The names enteramine (which indicates only one source) and serotonin (which suggests one action) are not satisfactory, and the chemical name 5-hydroxytryptamine (5HT) is now widely used.

### DISTRIBUTION IN THE TISSUES

5HT occurs widely in nature (Erspamer, 1954). Its presence has been demonstrated in many body tissues and fluids of man and animals.

It is found in the alimentary canal (in the mucosa of the stomach and the small and large intestine), in the spleen, glandular tissue, and in carcinoid tissue.

It is present in the blood serum, there being less in older persons than in young persons. The platelets contain 5HT but this may be incidental; it is not decided whether 5HT is synthesized and incorporated at the site of platelet formation, or whether it is taken up by them in the circulation. The platelets act as a circulating storehouse for 5HT and the other vaso-active amines, protecting them from amine oxidase.

In the brain 5HT is present in the grey matter, not in medullated nerve fibres, and especially in parts associated with the autonomic nervous system and the area postrema (Amin *et al.*, 1954; Paasonen and Vogt, 1956).

5HT and its derivatives are present as normal excretion products in the urine.

5HT has been found in the skin of amphibia (Erspamer and Boretti, 1951), in wasp venom (Jaques and Schachter, 1954), and in the stinging nettle, *Urtica dioica* (Chesher and Collier, 1955), but there is little or none in bee venom (Erspamer, 1954).

The content of 5HT in the tissues of various animals (more than 30 species) is known; details are given by Erspamer (1954). The data are important in the interpretation of the biological significance of 5HT, since actions of the compound which are to be considered physiological are those produced in the animal by doses not more than the total amount of 5HT in the animal; all other actions have to be considered pharmacological.

### IDENTIFICATION AND QUANTITATIVE ESTIMATION

The demonstration of 5HT in various biological materials has been accomplished by chemical isolation, by colour reactions, and especially by paper chromatography and pharmacological methods.

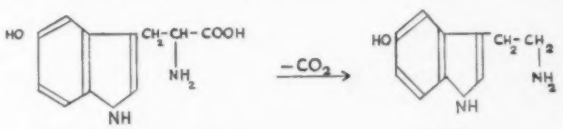
The contraction of vascular, intestinal and uterine muscle has been employed extensively for bio-assay of 5HT (Page, 1954).

The contractile response of the fresh isolated uterus of the atropinized oestrus rat has been used (Amin, A. H. *et al.*, 1954; Barkhan, 1955), and lysergic acid diethylamide (LSD) has also been employed in the test, since it is a specific antagonist of 5HT on this tissue. Stimulation of the isolated heart of *Spisula solida* (*Mactra solida*) and other molluscs has been used, 0·1–1 microgram per litre being effective (Gaddum and Paasonen, 1955).

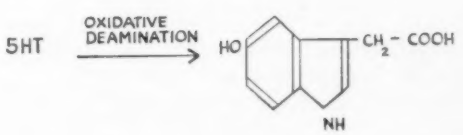
However, chemical and chromatographic and other tests are now being increasingly used to determine the presence of 5HT in the blood serum or of its excretion product, 5-hydroxy-indole acetic acid (5HIAA), in the urine. These tests are considered later in connection with the clinical diagnosis of 5HT-producing tumours.

### BIOSYNTHESIS AND FATE

It would appear that 5HT is manufactured from tryptophan; this amino acid is oxidized to 5-hydroxytryptophan, which is then decarboxylated to 5HT. 5HT itself is rapidly oxidized to 5HIAA, apparently in its passage through the lungs. 5HT resembles several other substances in being a substrate of amine oxidase.




5 HYDROXYTRYPTOPHAN 5HT




5HIAA

5HIAA is the main break-down oxidation product and it can be demonstrated in normal and abnormal amounts in the urine by a number of quantitative and qualitative tests (Editorial, 1955). The normal daily output in man, according to various workers, is from 3 to 10 mg. Such large amounts of 5HIAA excreted in man and in certain animals (but not in all) suggest that the metabolism of endogenous 5HT is very intense, and that 5HT may not be the only precursor of 5HIAA.

## PHYSIOLOGY

The functions of 5HT under physiological conditions are not definitely established.

It has been suggested that it may play a role in:

Haemostasis: 5HT is liberated from platelets during clotting and may influence haemostasis by producing local vascoconstriction.

Whether it plays any part in preventing bleeding tendency remains to be decided; in thrombocytopemia the value of blood 5HT may be low, but the amounts found are variable (Barkhan, 1955). Apart from abnormality in platelets there may be vascular defects in bleeding disorders; 5HT may prevent haemorrhage by increasing capillary resistance.

5HT constricts mesenteric, muscle, and skin arteries and arterioles, possibly in the regulation of vascular tone and thus of arterial pressure.

Its presence in the gastro-intestinal tract suggests that it plays a role in the muscular activity (control of peristalsis) or vascular control of this system.

5HT appears to have some specialized function in maintaining a normal central nervous system. It has been suggested that some mental disorders may be due to deficiency of 5HT, and that a 5HT-like compound may be of value in the treatment of conditions similar to schizophrenia. A comprehensive article by Woolley and Shaw (1954) deals with the neurophysiological aspects of 5HT and its significance in mental processes; they suggest that lack of 5HT in the central nervous system results in mental disorder.

5HT may be important in regulating the intrarenal circulation and kidney function and this is considered by Erspamer (1954) and his co-workers to be the physiological action of the amine.

5HT is released, as histamine is, in anaphylaxis, possibly from the platelets (Humphrey and Jaques, 1953).

It may be concerned in the effects of coronary thrombosis, and traumatic shock.

The excessive secretion of 5HT by argentaffin tumours is the basis of an interesting clinical syndrome, and it appears to be released in pulmonary embolism; these clinical disorders are considered later.

## PHARMACOLOGICAL ACTIONS

Many of the actions of 5HT have been reviewed in detail by Erspamer (1954) and by Page (1954). A striking feature about 5HT is its great activity on isolated tissues and its relatively weak pharmacological action when given intravenously. Its most characteristic and important pharmacological action is stimulation of smooth muscle, some muscle preparations being especially sensitive, for example the renal vessels.

### *Cardiovascular System*

The isolated artery of the sheep, ox and dog, and the perfused vessels of the rabbit's ear, contract when 5HT is applied.

In the cat it causes a rise in the pulmonary arterial pressure; it has a vasoconstrictor and also a bronchoconstrictor action in the cat's lungs, which is antagonized by lysergic acid diethylamide (LSD) (Gaddum *et al.*, 1953).

The vascular actions are antagonized by ergotamine, dibenamine, and yohimbine, whereas cocaine potentiates them. In certain vascular beds 5HT is more potent than adrenaline as a vasoconstrictor and in others it is less potent, according to Furchgott, 1955. There is evidence from the use of various blocking agents that certain specific motor receptors are directly activated by 5HT and are distinct from adrenergic motor receptors. It is possible that in certain cases 5HT may have an indirect action through the release of acetylcholine, noradrenaline, or adrenaline, for example in increasing the coronary blood-flow. A depressor effect on systemic blood pressure may be due in part to liberation of histamine; on the other hand the strong vasoconstrictor action of 5HT may overcome the histamine vasodilatation (Feldberg and Smith, 1953).

In the intact animal various direct and reflex cardiovascular actions occur, so that the effect on the systemic blood pressure is variable and unpredictable. The action is moderate and of doubtful physiological significance—hypotensive, hypertensive and mixed responses occur, and are probably due to a pharmacological action of 5HT.

Intravenous injection in man produces a short period of hyperpnoea and a transient fall in systemic blood-pressure followed by a rise or a fall according to the dose and the degree of neurogenic vasoconstrictor tone. The degree of response is very variable (Singer and Sternlieb, 1955.)

Injection of 5HT into the human brachial artery produces constriction of vessels in the forearm and hand causing resistance to blood flow and a dilatation of other vessels which results in marked flushing of the skin (Roddie *et al.*, 1955).

### *Other Smooth Muscle*

5HT causes contraction especially of rat uterus, guinea-pig ileum, and vessels in the (perfused) rabbit's ear, the actions on the uterus and ear being specifically inhibited by LSD (Gaddum and Hameed, 1954).

Local anaesthetics also antagonize the stimulant action of 5HT on various smooth-muscle preparations (Sinha and West, 1953).

The virgin uterus in the intact cat is relaxed by 5HT; the nictitating membrane and the pupillary sphincter contract. Stimulation of the intestine is due to a direct action on the muscle and is apparently cholinergic in action, since the effect is blocked by atropine (Rocha e Silva *et al.*, 1953).

*Central Nervous System*

5HT is normally present in the grey matter of the brain (indicated above).

It has been suggested that the changed mental status following the administration of lysergic acid diethylamide (LSD) (and the disease schizophrenia) may be the result of interference with the function of 5HT. However, although an interaction between LSD and 5HT has been demonstrated in man (Rodnight and McIlwain, 1956)—for example a partial but consistent fall in the excretion of 5HT after intravenous LSD—its specificity, directness, and possible relation to mental phenomena remain to be investigated.

The central nervous sedative action, and possibly certain other actions, of reserpine have been attributed in part to the release of 5HT (Pletcher *et al.*, 1955, 1956).

The actions of ephedrine and amphetamine compounds may possibly be connected with 5HT, since they inhibit the enzyme, amine oxidase, which inactivates 5HT.

5HT has been injected into the ventricles of the human brain (through the rubber bung of a cannula screwed into the frontal bone). The patients were chronic psychotics who had been ill 3-25 years. After injection the patients became pale, perspired, were active or restless, talked readily, and after several weeks showed clinical improvement. They became employable and interested, improved their habits and appearance, and spoke more rationally (Sherwood, 1955).

Sensory nerves: When applied to the exposed base of blistered skin of man small amounts of 5HT in concentrations as low as $10^{-8}$ cause pain (Armstrong *et al.*, 1952).

*Kidney*

The action of 5HT on the circulation and function of the kidney is considered to be the physiological action of the amine (Erspamer, 1954). It has an antidiuretic (hormonal) action in man and several other mammals. The effects appear to be produced by alteration of the intrarenal circulation, e.g. by reduction of glomerular filtration rate from constriction of the afferent glomerular vessels, or possibly from partial diversion of the blood ('shunt') from the cortex to the medulla.

In hydrated rats 5HT injected subcutaneously reduces the diuresis by causing vasoconstriction of the afferent glomerular vessels and reduction of intraglomerular hydrostatic pressure. It may also produce a reduction in the absolute excretion of chlorides, thus differing from vasopressin, which is antidiuretic but causes an increase in the excretion of chlorides (Erspamer and Correale, 1955).

However, from studies on conscious dogs it was concluded by Abrahams and Pickford (1956) that there are several explanations for the antidiuretic action of 5HT, e.g. alteration of the general blood pressure, or release of antidiuretic hormone from the posterior pituitary body, and that it is not a specific renal (vascular) hormone.

## CLINICAL

### THE MALIGNANT CARCINOID SYNDROME

Malignant carcinoid tumours (argentaffinomas) producing a vaso-active substance and associated with a peculiar syndrome are being increasingly recognized since the comprehensive investigations of the Swedish workers Thorson *et al.* (1954), and case reports by others, for example, McKusick (1956), Sjoerdsma *et al.* (1956).

The enterochromaffin, argentaffin, argentophile or argyrophile cells of the intestine are the parent cells of these carcinoid tumours. The existence of cells in the gastro-intestinal tract that take up silver stains has been known for a long time; the cells reduce silver nitrate and stain black, hence the various names. The cells were first discovered by Heidenhain in 1870, in the stomachs of rabbits and dogs, and he described their chromaffin nature (strong affinity for chromium salts). They are present not only in the gastro-intestinal tract, but also, for example, in the gall bladder and the pancreas. Incidentally the alpha cells of the islets of Langerhans have similar staining properties with silver stains.)

It is believed that these argentaffin cells have an endocrine or enzymatic action, and that 5HT (and glucagon) are in part probably secreted by them. Cyanocobalamin has also been shown to be present in extracts of these cells (Singer and Sternlieb, 1955).

Argentaffinomas (carcinoid tumours) comprise approximately 1% of all neoplasms in the gastro-intestinal tract, and occur mostly in the region of the ileocaecal valve. They may cause obstruction, e.g. in the appendix or in the terminal part of the ileum. They are yellow or light-brown in colour, owing to their high lipoid content or to the interaction of 5HT and formalin (Gibbons, 1955).

Large amounts of 5HT have been found in the tumours—as much as 2·5 mg. or more per gram of fresh tumour tissue, and in the blood of patients with this metastasizing carcinoid, e.g. 12 micrograms or more per ml. of serum (normal value up to about 0·3 microgram per ml. of serum). Secretion from metastases can occur after removal of the primary tumour (Pernow and Waldenstrom, 1954).

The principal features of the syndrome have been described by various authors (Biorck *et al.*, 1952; Thorson *et al.*, 1954; Gibbons, 1955; McKusick, 1956). They include the following:

*A.* Malignant carcinoid tumours, chiefly in the small intestine (but occurring anywhere from stomach to rectum), with slow progression, and with metastases in the liver and other intra-abdominal organs.

*B.* Dependent oedema, frequent watery stools, abdominal pain, and borborygmi, occur; more rarely, ascites and pleural effusion. The diarrhoea may be due to hypermotility of the intestine caused by 5HT, but previous resection of a portion of the bowel may occasionally be the cause.

*C.* Peripheral vasomotor features occur from dilatation of the smaller skin vessels; sometimes there are

telangiectases, e.g. on the face, or pellagroid skin vessels. Peculiar patchy reddish-blue discolouration of the skin also occurs, often intense and in periodic attacks, giving the appearance of plethora and partial or total cyanosis (in the absence of polycythaemia). Such striking skin changes of flushing and discolouration, irregular in distribution and colour, appear to be due to degrees of contraction and dilatation of precapillary arteries and capillaries. During a generalized red flush the heart rate may increase and a large pulse-pressure occur. In a menopausal woman it will be necessary to distinguish the flushing caused by increased secretion of 5HT from that due to diminished ovarian secretion. The association of flushing with meals or with certain procedures (see below) has been observed by many patients. The *mechanism* of the cutaneous phenomena has not been properly established. They may be caused by the vasoconstrictor action of 5HT, by the release of histamine by 5HT, or by an action of 5HT on the diencephalon. Pellagroid skin changes may be the result of a conditioned nicotinic-acid deficiency, as described below.

*D.* Pulmonary stenosis of the valvular type, and tricuspid regurgitation, occur; the other heart valves may also be involved. Cyanosis may, however, actually appear in this syndrome years before signs of congestive heart failure, as the result of the peripheral vasomotor features described above.

*E.* Bronchoconstriction may result in attacks of 'asthma' of unusual type in which cyanosis and exanthema of the face and body occur, with sudden dyspnoea.

The features of the syndrome are attributed to the secretion of large amounts of 5HT, which then act directly or by some other mechanism. Since there is a relationship between tryptophan and nicotinic acid some of the cutaneous, intestinal and mental disturbances in the syndrome may be the result of nicotinic-acid deficiency induced (conditioned) by the carcinoid material, which converts large amounts of tryptophan to 5HT.

*Diagnosis*

The clinical diagnosis of argentaffinoma is based on the signs and symptoms described above. Radiography aid in the demonstration of tumours of the small intestine. Mechanical stimulation or manipulation of the tumour, enemas, or pressure on the liver, may induce characteristic attacks from the release of 5HT; sometimes the stimulus has presumably been the taking of alcohol or food (Bleehen, 1955).

Histamine given intravenously has been used to induce the release of 5HT in patients with suspected carcinoid tumour (Daugherty *et al.*, 1955), in the way it is used in the diagnosis of phaeochromocytoma.

Chemical and chromatographic screening tests for argentaffinoma have been developed (Editorial, 1955), which can only be briefly considered here.

*Blood.* The 5HT content of blood serum may be estimated by chromatography; in normal persons there is 10-30 micrograms per 100 ml. according to one method (Udenfriend *et al.*, 1955a). By biological assay using the isolated rat-uterus the normal serum-5HT activity has been estimated as ranging from 4·4 to 24·7 micrograms per 100 ml. (mean value 9·8—Barkhan, 1955).

*Urine.* Simple qualitative colour tests are available, based on the presence of 5HIAA in the urine (Sjoerdsma *et al.* 1955; Hansen and Serin, 1955). This metabolite of 5HT may also be detected by extraction of the urine and the use of paper chromatography (Gibbons, 1955).

According to Udenfriend *et al* (1955b) a quantitative colorimetric test for 5HIAA reveals normally 2-8 mg. per 24-hour sample of urine. Others have estimated that the normal amount of 5HIAA excreted daily is 5-10 mg. In patients with argentaffinoma as much as 65-350 mg. may be excreted daily. A rapid chromatographic test for estimating 5HIAA and 5HT which takes 1 hour to perform has been described (Curzon, 1955).

Since tryptophan is a source of 5HT and hence of 5HIAA (Sjoerdsma *et al.*, 1956) the estimation of these substances in patients with carcinoid tumours, strictly speaking, necessitates that the intake of tryptophan should remain constant during periods of analysis.

## PULMONARY EMBOLISM

Many of the circulatory symptoms of pulmonary embolism, even from relatively small emboli, appear to be the result of the release of 5HT from the clot in the vessel and from the infarct (Editorial, 1956). Heparin has been used to counteract some of the action of the 5HT.

There is still much to be learned about the physiological significance of 5HT and its effects in various diseased states. There are indications for the use of drugs antagonistic to 5HT in the diagnosis or treatment of certain conditions in man. Satisfactory anti-5HT agents for clinical use remain to be discovered.

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# A PRELIMINARY REVIEW OF THE USES OF CHLORPROMAZINE IN PSYCHIATRIC DISEASES*

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Amongst the recent advances in psychiatric treatment by means of drugs, chlorpromazine is playing an ever increasing and important role. It was first used clinically by Laborit and Hugenard in 1951 in relation to anaesthetics and later (1953) by Delay and Deniker[1] in psychiatry. It has been adopted generally for virtually every known psychiatric illness and varying opinions have been expressed concerning its efficacy. At the Oranje Hospital it has been in active use for the past 8 months with varying—sometimes startling—results. It has been tried alone or in combination with other drugs or electroconvulsive therapy (etc.).

*Clinical Effects*

According to reported observations the most striking clinical property of chlorpromazine is its ability to induce somnolence leading to a state of detached unconcern, yet without interference with mental ability. Lomas[2] points out that even when a soporific state is produced the patient is as easily roused as from normal sleep, and tends to fall asleep only if he has no external interests at the time. Thus it is entirely different from any of the barbiturates or other sedatives in common use. Its indications in psychiatry were originally based on this ability to induce somnolence and ease tension, and thus to secure a so-called 'chemical leucotomy'. Numerous investigators have applied it in states of increased psychomotor activity, whether of manic, schizophrenic, epileptic or other origin. All seem to be agreed that a tranquillizing effect, whether temporary or permanent, can be produced in as short a time as a few days by an injection of 50 mg. 8-hourly. At the same time various observers have noticed concomitant improvement in behaviour, appetite and sleep with a resulting increase in weight.

In addition to the functional conditions chlorpromazine has been found to be of use in certain organic disorders (Cohen[3]); e.g. in delirium tremens, for agitated senile arterio-sclerotics, for post-encephalitics, and in post-traumatic personality disorders. This we have confirmed.

In the psychoneuroses conflicting opinions have been expressed, Some, e.g. Winkelman[4], believe that it can reduce severe anxiety and diminish phobias and obsessions while Cohen, agreeing to some extent, points out that the results are disappointing in hysteria, hypochondriasis, the usual depressions, and obsessive-compulsive and phobic neuroses. The weight of opinion seems to be that its value in the psychoneuroses is limited.

Davies[5] states that it controls aggressiveness *per se* and in various grades of mental deficiency, leading to improved behaviour and thus easing the nursing problem. Others have found that the discontented aggressiveness often associated with paranoid conditions is modified or considerably relieved, even though the paranoid constitution itself is unaffected.

Seager[6] has reported its use in elderly psychotic women and found it to be efficacious in 71% of his cases.

Gatski[7] has used it in the treatment of acutely disturbed and acting-out maladjusted children, and maintains that they became more tractable and could learn to conform to the norm with greater ease.

An interesting report is that of Benda and Klein,[8] in which they discuss 4 cases of status epilepticus which responded to the intravenous use of the drug after the usual methods had failed. This has been our experience on 2 occasions.

Fazekan *et al*[11] have used it in the management of acute alcoholism and post-alcoholic states. The major benefit was in the control of excitement and anorexia.

## ORANJE HOSPITAL: INDICATIONS AND RESULTS

At the Oranje, Hospital we have used chlorpromazine in the form of Largactil. The drug has been used from

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2 aspects, viz. (1) in the treatment of clinical entities, and (2) in the management of individual symptoms irrespective of the diagnosis.

1. *Treatment of Clinical Entities.*

In the manic depressive group very promising results have been obtained in the manic phase, either alone or in conjunction with ECT. We have found that the number of shocks required to control the hyperactivity of the manic phase is considerably reduced by the concurrent use of chlorpromazine. We have found that, to control an acute case of mania, as many as 2 shocks *per diem* for 5 days or more were necessary; since using chlorpromazine we have found that 2 shocks are all that is necessary to bring this phase under control. As a result of the experience we consider that the major indication for the use of chlorpromazine is in the manic phase of the manic-depressvie psychoses.

Amongst our cases, J. R. E. duP., ME* 3209, who has been a patient on several occasions and was treated previously with ECT, we found that on his last admission ECT was unnecessary, and he was brought under very rapid control with chlorpromazine only. In fact, within 3 days of admission his severe increase in psychomotor activity was greatly reduced, and within 10 days he was well on the way to a full remission.

In other similar cases a regime of 2 or 3 shocks on alternate days, with oral chlorpromazine and small doses of phenobarbitone or amytal, has rapidly brought the patent under control with a minimum of risk and nursing requirements.

Furthermore as regards the chronic manic who displays periodic exacerbations of his condition, and who was a severe nursing problem and required frequent repeat administrations of ECT, we have found that the shock treatment could largely be replaced by chlorpromazine. In 5 cases of the chronic mania type, 3 have become fit for leave of absence, and 2 are much more easily managed and less burden on a depleted nursing staff. Of these cases C.A.D., FE† 2092, diagnosed as chronic hypomania, and who, until put on chlorpromazine 4 months after admission, was markedly overactive, inconsequent and difficult to manage, settled down very quickly. Her relatives were most diffident in taking her on leave, and it was only after a struggle of some 6 months that we eventually succeeded in persuading her daughter to give her a trial. A letter written by the daughter some 2 weeks after her release is extremely interesting; she writes, 'You will be pleased to know that Mrs. D. continues to keep well'. We feel that should she display signs of relapse, early therapy should obviate the necessity for readmission.

We believe that, as a group, the senile psychoses, with or without hypertension or arterio-sclerosis, benefit considerably by the use of chlorpromazine. The aimless, restless and interfering patient is rapidly brought under control. The drug eliminates or reduces the necessity for other forms of treatment and lessens the amount of sedatives. It eliminates the hazards of ECT given in old age. We have found in some cases that its calming effect is enhanced if it is preceded or combined with intensive nicotinic-acid therapy and supplemented by barbiturates of moderate action. Although this series comprises only a small group, it is felt that the results are important. All these patients were well known to the staff for a long period, and therefore the easing of symptoms stood out clearly against a very definite background, after the institution of chlorpromazine. One case, C.J.R.L., ME 3220, relapses into a restless and mildly agitated state, whenever his treatment is discontinued for any length of time. This state responds within 7 days to 2 tabs. *tds* orally, and thus instead of being a constant burden he becomes an easily manageable individual. Another case, H.V.T., FE 2079, becomes resistive and confused, and requires much attention from every aspect. On 150 mg. daily she improves sufficiently to eat on her own, she becomes fairly cooperative, and conversation with her becomes possible. The third case, A.J.L., ME 3229, did not show the same measure of improvement, but his resistiveness to attention became less. Unfortunately his result was blurred by the advent of jaundice and fever.

As already mentioned, chlorpromazine has been used in an attempt to bring status epilepticus to an end. On 2 occasions we have used it intraveneously after other methods had failed, and in both cases the seizures were brought to an end—in one case after 3 more seizures, and in the other after 5. However, as this method is still in its infancy the more recognized treatments should still be depended upon, and chlorpromazine should only be used as a last resort. Both our cases died, the one after some weeks and the other after some days, both from intercurrent disease (pneumonia).

As regards possible complete cure, as compared with remission in a manic episode, we feel that we obtained this result in a patient with a post-traumatic psychosis. This patient, a male Native J.R., MN 6041, received several blows on the head and suffered from severe cerebral injuries. On admission he was confused, excited, disorientated and incoherent. He was tried on ECT. He was given intensive nicotonic-acid therapy, and intensive sedation. The ECT was used in an effort to control the excitement. After 4 months, having shown no signs of improvement, he was tried on chlorpromazine, and within 3 weeks there was a marked improvement. He has since been discharged, recovered, and has returned to his former employment.

Our experience with chlorpromazine treatment of the psychoneuroses is limited; we only had 2 suitable cases, and in both the beneficial results were limited. In both there was considerable anxiety, hypochondriasis and a lack of self-confidence. Both cases required other treatments and, in our opinion, the only value of chlorpromazine was that it helped the 2 patients to settle down to their surroundings more easily.

2. *Management of Individual Symptoms.*

In spite of the apparent contra-indication of chlorpromazine in epilepsy—it is thought by some to increase the tendency to seizures—we have tried it in a group of 7 Native males and 2 European females with the object of reducing the aggressive content, irritability and

* ME = Male European.

† FE = Female European.

restlessness. This experiment has been carried out over an average period of 10 weeks with a maximum dose of 150 mg. per day, and the customary anti-convulsants were continued. Although they all showed an increased tendency to drowsiness, the following features were observed:

In 5 patients the numbers of seizures remained unchanged, in 3 cases there was a slight reduction in the number of seizures in comparison with a similar period before treatment, and in 1 case the number of seizures was increased, though not significantly.

There was no change at all in the aggressiveness, irritability and restlessness in 4 cases. In 5 cases there was a moderate improvement, in that their symptoms were less severe and of shorter duration, and for this one reason we consider it necessary to carry out further trials with considerably larger doses over a longer period of time.

Chlorpromazine has already been shown to be of value in manic and senile conditions *per se*; we have also tried it for excitement in schizophrenic conditions but, possibly because the dose was too small, our results have been disappointing. The treatment, however, was only used for short periods when a patient was particularly impulsive or excited.

In 10 cases of chronic schizophrenia, mostly showing delusions, restlessness, impulsiveness and sleeplessness, there was no change in 3 cases, some degree of improvement was noticed in 6 cases but not sufficient to warrant enthusiasm—it would appear from the recent work of Delay and Deniker that doubling of the doses may prove more beneficial—and in 1 case the patient displayed unexpected emotion in the way of tearfulness and depression. We have used chlorpromazine in some paranoid conditions and the patients have shown a lessening of their unpleasant and aggressive attitudes, though no change in the mental content. In one case, C.A.S., ME 3179, who before its use was extremely abusive, angry, and markedly suffering from persecutory delusions, his delusions changed their character with this treatment; he became amiable and grandiose, but since cessation of treatment his delusions have reverted to their former state.

## REVIEW OF CASES

In Tables I and II a review is given of cases who received fairly concentrated treatment with chlorpromazine (numerous other patients were given the treatment but are not included because they have been treated for too short a period).

### *Method of Dosage and Technique*

The chlorpromazine may be given orally, intramuscularly or intravenously:

Orally it has been our practice to give 25 mg. *tds.* increasing to 250 mg. daily and it can be continued for as long as necessary, provided no complications occur.

Intramuscularly 50 mg. every 8 hours for 2—3 days. The injection is very painful and it is advisable to change over to the oral regime as soon as possible.

We have used the intravenous method only for status epilepticus. The dose must be diluted to the extent of 50 mg. in 10 c.c. of sterile water and it must be injected very slowly.

It is our view that much larger doses can be safely used and it is our intention to intensify the treatment in the schizophrenic group. Several workers have already given as much as 800 mg. daily, and more.

### *Toxic Action and Side-effects.*

Toxic symptoms did not occur very frequently in our series. This may be due to the fact that our periods of treatment were comparatively short and the dosage moderate. Amongst the toxic effects we have noticed are:

1. *Jaundice.* This occurred in one case, an old man 80 years of age, who was very restless and confused, disorientated and difficult to manage. He was on 150 mg. daily for 4 weeks when symptoms first developed. He was reported as having had a syncopal attack, apparently as described by Lomas in the aged, and on the following day the symptoms of jaundice were obvious. A rise of temperature up to 100—101°F was recorded over the next 3 weeks. His recovery, although slow, was uneventful. He was treated with penicillin with the object of avoiding any intercurrent infection.

2. *Sudden drop of Blood Pressure.* In a patient with arteriosclerosis and hypertension (systolic blood pressure 190 mm. Hg), there was a sudden fall of 40 mg. at the end of the first day's treatment by intramuscular injection. He was extremely drowsy and unable to stand, but he could be roused. With a reduction in the dosage his untoward symptoms subsided, and treatment was continued by the oral route without further difficulty.

3. *Incoordination.* This occurred in a young patient who was a competent pianist, and was manifested by the fact that he became unable to carry out the finer movements necessary for the exercising of his talent. The incoordination was so mild that we did not interupt the treatment. (Goldman[9] describes a syndrome resembling paralysis agitans. In his mildest case he found some rigidity of the extremities, with stooping posture, and there is little doubt that this case of ours is a still milder example of this side-effect. In the severer types of this complication he describes characteristic pill-rolling tremor, changes in gait and speech, and salivation.)

Agranulocytosis has been described by Goldman,[10] Lomas[2] and others in chlorpromazine treatment of mental-hospital cases. We have not thus far encountered it. According to Lomas *et al*[10] toxic effects occurred in 7·4% of cases, viz. jaundice, blood dyscrasias, skin reactions, oedema, and epileptic fits. Thus a history of liver dysfunction or previous blood dyscrasia is an absolute contra-indication to treatment with chlorpromazine. An interesting fact referred to by Lomas *et al*[10] is that side-effects (in contradistinction to toxic effects) occur much less frequently in the psychotically disturbed than in others. These authors do not regard incoordination as a toxic effect, but rather as a side-effect. The following are the commonest side-effects: Tachycardia, dryness of mouth, constipation, pronounced increase in appetite (a factor we are at present

observing in one patient), gain in weight, and increase in the quantity of urine.

## CONCLUSIONS

The conclusions we have arrived at from our cases under treatment are as follows:

(*a*) Chlorpromazine is not a *curative* agent against any established psychosis (except perhaps in one case in which the post-traumatic confusion was cleared).

(*b*) It is an extremely valuable addition to our psychiatric armamentarium, and should play an important role in the reduction of admissions to mental hospitals in the senile group, and a reduction in the duration of manic phases, thus permitting of a shortening in the period of detention.

(*c*) It leads to an increase in the number of patients able to go on leave.

(*d*) It aborts attacks in frequently recurrent mania, or brings the attacks under more speedy control. It reduces the number of electro-convulsive shocks necessary in the more resistant cases.

(*e*) Perhaps its greatest benefit in these days of depleted nursing services, lies in its ability to ease the nursing problem, by the decrease in attention the restless patient usually demands.

(*f*) In schizophrenics and epileptics, very little actual benefit is achieved on the moderate dosage schemes we have used. In epilepsy, judging by the remarks of others, it may be contra-indicated and in fact should not be used except in conjuction with the anti-convulsants. Our conclusions (apart from high-dosage treatment) conform with opinions of other investigators such as Vaughan *et al*,[12] Lomas *et al*,[10] and Delay and Denikker[1].


## SUMMARY

A preliminary review of chlorpromazine treatment at the Oranje Hospital, Bloemfontin, is undertaken in this paper, and reference has been made to its value in the manic depressive, senile, schizophrenic and epileptic groups, from the aspect of both clinical entities and individual symptoms. The toxic effects are referred to. The conclusion is that it is a very valuable adjunct to psychiatric treatment in general.


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## POSTSCRIPT

Since this article was written several workers have experienced rather distressing symptoms in cases being treated with ECT and chlorpromazine or Serpasil, and a number of unexplained deaths have occurred.

# ADENOMA SEBACEUM WITH PSYCHOSIS IN A BANTU WOMAN


J. S. DU T. DE WET, M.B., CH.B.

*Assistant Physician Superintendent, Tower Hospital, Fort Beaufort*


The condition termed epiloia, Bournville's disease or tuberous sclerosis is probably still considered to be very rare in coloured races'.[1]

In 1955 a case of epiloia[2] was reported in a Bantu woman from the Grahamstown area. She presented all the main features of adenoma sebaceum, tuberous sclerosis and epilepsy with imbecility. It is interesting to report now, another case of adenoma sebaceum from the same area, yet apparently unrelated to the first one. This time the features of epilepsy and of tuberous sclerosis are not clearly evident. However, a good photograph was obtained and is printed here (Fig. 1) to illustrate the adenoma sebaceum.

## CASE RECORD

The patient J.M. (F.N. 4233) was admitted as an urgent case to Tower Hospital, Fort Beaufort on 6 February 1955 from Grahamstown, where she lives. She is married and has 4 children. According to her own statement she has had the condition of adenoma sebaceum since childhood and several of her relatives and children also have it.

Her husband stated that she was violent and threatening; that she attempted to assault people and that she was continually shouting and tried to run away. This condition was reported to have lasted for one week. She was said not to be epileptic.

On admission she was wildly excited, resistive and restless. If approached by anyone she became terrified, screamed and shouted. Her utterances were disconnected. If left alone she would often be quiet. She refused to eat in the presence of others, yet when left to herself she ate ravenously anything she could grab. There was no psychomotor retardation. This condition persisted for 2 days, when it subsided and she became rational quite suddenly.

Henceforth she was mildly depressed and irritable but quiet in behaviour and able to hold a conversation. She related that she had not been getting on well with a woman who was her neighbour and she admitted she had been thought to be disordered. Orientation in time and place was defective but she did not appear at all confused. She said she had been disturbed by the voices of unseen people, and that her neighbours accused her of being a witch. Her auditory hallucinations were extremely disturbing and made her panic-stricken so that she had the impulse to escape. No evidence of visual, olfactory or of other hallucinations could be

*Fig.* 1 Adenoma sebaceum.

elicited. She denied having suffered from similar disturbances previously. When she was questioned closely about events leading up to her admission it did not appear that she had an amnesia for the period of her acute disorder.

Her quiet behaviour continued for 1 month after admission but she remained mildly depressed, apparently as a reaction to her detention in mental hospital.

Tested on the Binet-Simon scale (official mental-hygiene individual scale from U.E. 68 amended 1927), she was found to pass all the tests from year 3 to year 6. At the 7-year level she failed Knox C, and could not copy a diamond correctly. At the 8-year level she failed 2 out of the 6 tests, being unable to count backwards from 20 to 1 or to repeat 3 digits in reverse order. At the 9-year level 2 of the tests were impossible to apply owing to her lack of education, and of the remaining 3 she only passed one (similarities test), and failed the 'Ball and Field' test, as well as the Knox D test. She failed the remaining tests in the scale which could be used at all in her case.

It may be concluded, therefore, that her mental age, according to this scale, is 7 years and 2 months. The average mental age of South African Natives on the Binet-Simon scale was found by Fick[3] to be approximately 10 years. Taking this as the usual level for South African Natives on this scale her IQ is approximately 70.

It seems probable, therefore, that she is a high-grade feebleminded individual, and this coincides with the impression formed by her nurses and attendants, most of whom have had wide experience of persons belonging to her social group.

Physical examination reveals no gross abnormalities apart from characteristic adenoma sebaceum and a flat pigmented vascular tumour the size of a shilling but oval in shape, situated on the left side of her face. just anterior to the ear.

No signs of tuberous sclerosis were seen in the skull radiogram.

No phakomata were detected on examination of the fundi and no visceral or other tumours or *peau de chagrin*. The adenoma sebaceum is very pronounced, as can be seen from Fig. 1; it is of a dusky purple colour.

## SUMMARY AND DISCUSSION

A case of adenoma sebaceum in a Bantu woman is reported. Signs of tuberous sclerosis were not seen on the skull radiogram and there was no evidence of epileptic fits. On admission she had an acute transient psychosis, with behaviour and affective disturbance as well as auditory hallucinations. When the psychosis had been spontaneously recovered from, the patient was found on testing to be feebleminded.

Her psychotic episode is thought possibly to have been epileptic in origin. As temporal-lobe lesions are now thought to be a cause of psychomotor epilepsy,[4,5] the presence of a sclerotic focus in this part of the brain has to be considered.

Electro-encephalographic and radiological investigations not available at this hospital, should be of value. Deep X-ray therapy[6] or treatment by surgery may then be indicated for the alleviation of a mental disturbance which may eventually prove to be paroxysmal.

I should like to thank the Commissioner for Mental Hygiene, Dr. I. R. Vermooten, and the Physician Superintendant of the Tower Hospital, Dr. L. R. Brumberg, for permission to publish this article.

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# TRAUMATIC ARTERIO-VENOUS ANEURYSM

G. G. AIREY, M.R.C.S., L.R.C.P.

*Umtata, Transkei*

It is not often that one encounters in civil life injuries which result in arterio-venous aneurysms. The following case may therefore be of some interest.

On 20 March 1956 a young Native male was admitted to the Sir Henry Elliot Hospital, Umtata, suffering from a gunshot wound. The entrance wound was at the level of, but medial to, his left anterior iliac spine, and the exit wound on the supero-lateral aspect of his right thigh about 3-4 inches distal to Poupart's ligament.

I was asked to see him a week later, when a pulsatile swelling was present, with a machine-like bruit, just distal to Poupart's ligament. It was decided to leave him for as long as possible in order to try and establish some collateral circulation. Four weeks elapsed before it was decided to operate, during which time the aneurysmal dilatation had increased only very slightly.

The operation was performed on 23 April. The first step was to do a laparotomy in order to sling the common iliac artery and vein on separate tapes, in view of the fact that no certain information was available about the exact level of the fistula or its extent. A long straight incision was then made extending distally from

Poupart's ligament for about 6 inches down the thigh. The femoral vein, femoral artery and profunda femoris were then exposed and tapes passed under each. The saphenous vein was cut and tied at its junction with the femoral vein.

Careful dissection revealed the following state of affairs: There was a fistula about an inch in length between the femoral artery and vein. Posteriorly, in the arterial wall there was a further opening continuous with a large sac burrowing deep to the sartorius and superficial to the rectus femoris, about the size of a tangerine.

The artery and vein were separated and the opening in the vein closed with interrupted mattress sutures of fine oiled dermalon. It was found impossible to suture the two openings in the femoral artery, which were parallel and separated only by 3 or 4 millimetres of tissue. Neither was there available either any polythene tubing or metal arterial tubes. The defects were situated just proximal to the bifurcation of the femoral artery and extended proximally for about 1½ inches in all.

It was therefore decided to ligate the femoral artery above and below the defects. All tapes were removed and both wounds closed.

On return to the ward the leg was kept cool.

The patient is now up and walking about and has no trouble with his leg. There is no oedema or pain and there have never at any time been any signs of gangrene.

My thanks are due to Dr. J. Hofmeyr, who asked me to see the case, and for his kind assistance at the operation. Also to Drs. Robinson and Bloch for their help during a somewhat tense morning.

## ANNUAL REPORT OF THE CHAIRMAN OF FEDERAL COUNCIL FOR THE YEAR ENDED 30 JUNE 1956

*Obituary:* It is with deep regret that we record the loss through death of the following members: Drs. P. Allan, A. J. Badenhorst, P. J. Booysen, J. F. Bosman, R. Burns, L. J. Coetzee, A. H. Cole, H. A. Dippenaar, P. K. Dixon, R. D. A. Douglas, A. E. Dreosti, F. du Toit, G. C. Field, E. Frankenstein, J. C. Gie, A. L. Gilbey, L. B. Goldschmidt, I. Isaacson, I. Kallmeyer, T. P. Oates, D. J. Malan, H. J. Malan, R. B. Malan, I. H. Mandelstam, L. J. J. Muller, R. N. Pringle, C. M. Rautenbach, J. F. Salinger, A. Sanders, M. Sheehan, D. J. van der Westhuizen, C. G. L. van Dyk, A. B. van Zyl, E. van Zyl, L. S. Williams.

*Membership.* During the past year there has been an over-all increase in membership of 120, the total membership now being 5,343. In addition there are 78 student members. Members are distributed as follows: Border Branch 186; Cape Eastern Branch 58; Cape Midlands Branch 200; Cape Western Branch 1,171; East Rand Branch 210; Griqualand West Branch 85; Natal Coastal Branch 497; Natal Inland Branch 183; Northern Transvaal Branch 524; Orange Free State and Basutoland Branch 359; Southern Transvaal Branch 1,359; South West Africa Branch 67; Transkei Branch 83; Unattached Members 328; Emeritus Members 25; Honorary Members 8.

*Honours.* During the year the Council has honoured 3 members of the Association by electing them to Emeritus Membership. They are Dr. A. J. Orenstein and Dr. R. L. Girdwood of Johannesburg and Dr. R. D. Kidd of Pietermaritzburg.

*Annual General Meeting.* The Annual General Meeting for the current year took place in Pretoria on 17 October 1955. At the conclusion of the formal business Dr. J. H. Struthers of Pretoria was inducted as President by Dr. L. E. Lane, the retiring President. The meeting was then adjourned until the evening when it was re-convened and combined with the opening ceremony of Congress.

*Congress.* The 40th South African Medical Congress was held in Pretoria from 17 to 22 October 1955. At the Opening Ceremony Dr. Struthers delivered his Presidential address. The Minister of Health was present and addressed the gathering and the Mayor of Pretoria welcomed the visitors to the city. A number of honours which had been awarded during the previous year were presented to the recipients. The scientific sessions were of a high standard and the Congress was thoroughly enjoyed by all who attended. The thanks of the Association have been extended to members of the Northern Transvaal Branch who were responsible for the efficient organization of a very successful occasion.

*Federal Council.* There have been 2 meetings of the Council in the year under review. The first of these was held in Pretoria on 13-15 October 1955 and the second took place in Vereeniging on 11-13 April 1956. The average attendance was 50 members. The Executive Committee has met on 3 occasions; 2 of these were on the days immediately preceding the Council meetings and the 3rd occasion was a special meeting held on 21 February 1956 in order to decide on matters affecting Contract Practice policy. The major part of the work of this committee has been conducted by correspondence.

*Committees of Council.* The Head Office and Journal Committee continues to render service in looking after the administrative and financial affairs of the Association. The provision of increased accommodation for the Head Office and Journal Staff is proceeding by the addition of 4 floors to Medical House, Cape Town. The building work is progressing and the alterations should be completed by October 1956.

The Federal Ethical Committee has had no work to do during the year under review.

The Central Committee for Contract Practice has continued to do a considerable amount of routine work and has dealt with a number of new applications for recognition. The Council has reviewed its policy regarding Contract Practice and has decided that the branches are primarily responsible for the contract practice work which is done within the Branch areas. It has made provision for liaison between the branches and has reconstituted the Central Committee, making provision for an executive body of that committee. It was also decided that all members of council would be *ex officio* members of their Branch Contract Committees and that an official would be appointed to act as a local Secretary in the Transvaal. The tariff of fees for approved Medical Aid Societies has been revised and will probably come into operation on 1 January 1957.

*The Parliamentary Committee* has continued to watch the interests of members so far as legislation is concerned and has taken up with the legislative or the Government department concerned such matters as have come to its notice. An amendment to the Medical Dental and Pharmacy Act designed to control dispensing by doctors led to considerable activity.

The Workmen's Compensation Act Sub-Committee has been busy with the revision of the W.C.A. Handbook and has had many conferences with the Commissioner. It is hoped that the new tariff will shortly come into force.

*The Sub-Committee on the Economics of Medical Practice* has reported and will attempt to establish a medical aid society, in the Transvaal at first, along the lines suggested in the plan which was put forward.

The various other Committees appointed by Federal Council for special purposes have done useful work in the spheres allotted to them.

*Journal.* The weekly publication of the *South African Medical Journal* continues to meet with success as does the Association's quarterly journal, the *South African Journal of Laboratory and Clinical Medicine.* The Hamilton-Maynard Memorial Medal was presented to Dr. A. P. Blignault for his paper 'Electric coma treatment of mental disorder' and Dr. I. M. Hurwitz was awarded the Leipoldt Memorial Medal for his paper 'What can be done for Senescents'. These presentations were made at the Pretoria Congress.

*Branches and Divisions.* These continue to hold regular meetings and serve a useful purpose in bringing members together. No new Branches or Divisions have been formed during the current year.

*Groups.* These have continued to perform the tasks for which they were established, although there has recently been criticism that the Groups were undertaking work which should be the prerogative of Branches.

*World Medical Association.* The Ninth General Assembly of the World Medical Association was held in Vienna during September 1955. The Association's official delegate to the Assembly was Dr. A. I. Goldberg of Cape Town.

*Finance.* The accumulated funds of the Association increased by £1,315 during 1955 and they now stand at £33,724.

*Benevolent Fund.* At the end of 1955 there were 22 beneficiaries to this Fund. During the year ended 31 December 1955 grants totalling £2,437 6s. 0d. were made, and at the end of the year the accumulated funds stood at £41,984. Following a request made at the last Annual General Meeting the grants were increased during 1956 by an average of 25%.

*Library Grants.* Grants of £250 were made during 1955 to the Libraries of the Universities of Cape Town and the Witwatersrand. Early in 1956 a meeting of librarians was called and certain recommendations were made to Federal Council. As a result it has been agreed to provide assistance to the medical-school libraries at Pretoria, Durban and Stellenbosch when these are able to cooperate in a full library service scheme for members of the Association.

*Medical Agencies.* The two agencies maintained by the Association in Cape Town and Johannesburg have both shown an increase in service to members, who are asked to make full use of the facilities which are provided.

*Medical Insurance Agency.* There has been a slight recession in the amount of work undertaken by this department, although it is still well supported. The question of insurance cover against charges of malpraxis is one which has received attention by Federal Council and negotiations are at present proceeding in this regard. Members are urged to make use of the facilities offered by the Association in connection with all forms of insurance and are reminded that the activity of this agency adds to the Association's funds by means of the commissions earned.

*Conclusion.* On behalf of the Council I would thank all who have contributed to the work of the Association during the year under review. Numbers of honorary officials and members of committees have rendered valuable service and I would also record appreciation of the loyal cooperation of the Association's full-time staff. Although changes are inevitable from time to time it should be mentioned that the Secretary, Dr. Tonkin, and the Committee Clerk, Miss Olsen (Mrs. Eberlein), have both served the Association for over ten years.

A. W. Sichel
*Chairman of Council*

Cape Town
July 1955

## OFFICIAL ANNOUNCEMENT : AMPTELIKE AANKONDIGING

### APPOINTMENT OF EDITOR

Applications are invited for the post of Editor of the *South African Medical Journal.* Applicants must be registered medical practitioners having knowledge and experience of medical journalism. A knowledge of languages will be a recommendation. The salary attaching to the post is on the scale £1,800×60—2,400, plus cost of living allowance of £352 for married men and £176 16s. 0d. for unmarried persons. (£100 of this allowance will be consolidated for pension purposes). The commencing notch will be according to experience, at the discretion of the Federal Council.

In addition to the Association's official *Journal*, the successful applicant will be required to edit the quarterly '*South African Journal of Laboratory and Clinical Medicine*'. He will also be required to join the Association's Superannuation Fund.

Applications, together with testimonials and a certificate of health, should be addressed to the undersigned to reach him before 31 August 1956.

Medical House
35 Wale Street
Cape Town
19 May 1956

A. H. Tonkin
*Secretary*

### AANSTELLING VAN REDAKTEUR

Aansoeke word ingewag vir die betrekking van Redakteur van die *Suid-Afrikaanse Tydskrif vir Geneeskunde.* Applikante moet geregistreerde geneeshere wees met kennis en ondervinding van die geneeskundige joernalistiek. 'n Kennis van tale sal 'n aanbeveling wees. Die salaris aan die pos verbonde is op die skaal £1,800×60—2,400, plus 'n duurtetoeslag van £352 vir getroude mans en £176 16s. 0d. vir ongetroude persone. (£100 van hierdie toeslag sal vir pensioendoeleindes by die salaris gekonsolideer word.) Die beginsalaris sal na goeddunke van die Federale Raad met inagneming van vorige ondervinding vasgestel word.

Die applikant sal verwag word om benewens die redaksie van die Vereniging se amptelike *Tydskrif* ook dié van die kwartaalblad *'Suid-Afrikaanse Geneeskundige Tydskrif vir Laboratoriumen Kliniekwerk'* op hom te neem. Hy sal ook by die Vereniging se pensioenfonds moet aansluit.

Aansoeke, vergesel van getuigskrifte en 'n gesondheidsertifikaat, moet aan die ondergetekende gerig word om hom vóór 31 Augustus 1956 te bereik.

Mediese Huis
Waalstraat 35
Kaapstad
19 Mei 1956

A. H. Tonkin
*Sekretaris*

## RADIO-ACTIVE COBALT BOMBS AND SUPER-VOLTAGE THERAPY

MAURICE WEINBREN, B.Sc., M.R.C.S., L.R.C.P., F.F.R., D.M.R.E.

*Johannesburg*

In an article on this subject in the *Journal* of 23 June[1] Dr. L. Cohen purports to discuss and refute the points made in my article[2] on the same subject in the *Journal* of 2 June. The discussion in the lay press and the demand for super-voltage therapy and large radio-active bombs has continued, and one therefore feels compelled to answer Dr. Cohen's criticism.

His opening gambit—'The undeniable fact that many patients, not excluding doctors, go overseas for treatment, suggests that we are not at all satisfied with the standard of radiotherapy now available here'—indicates the type of reasoning he adopts. Patients who can afford it go overseas not only for radiotherapy, but also for surgical and medical advice, particularly as Johannesburg is now less than 24 hours away from Europe. It may well be that patients go overseas not because they are dissatisfied with the machine, but because they may rightly be dissatisfied with the man behind the gun. It cannot be denied that some of the conditions for which patients go overseas for radiotherapy require vast experience of the condition to be treated and not merely a large machine to treat the condition. It is now established that in the recent much-publicized case of the little girl the patient was sent to London for treatment by Sir Stanford Cade, and not for treatment with the radio-active cobalt bomb, which indeed she did not receive.

Has Dr. Cohen any figures to indicate that the numbers going overseas have increased because super-voltage therapy of the multi-million-volt type has become available in Great Britain within the last few years? How can one draw a conclusion on the value of radiotherapy merely because a few privileged individuals

are enabled by rapid transport conditions to go overseas to seek advice?

Super-voltage therapy was not condemned in my article, and nothing was said to justify the statement 'The ideas expressed in this paper are, in fact, at variance with almost all enlightened opinion throughout the world'. On the contrary, in 1947 I ordered a 2-million-volt machine but had to cancel the order because I could not get the radiotherapists and physicists to operate the unit safely. This is the whole crux of the matter. Apart from this, the views I expressed on the value of super-voltage radiation coincide with those of Dr. Constance Wood in her presidential address to the Royal Society of Medicine, Radiological Section, 1953.[8]

## SUPER-VOLTAGE THERAPY

If super-voltage therapy is as essential as Dr. Cohen maintains, and gives such markedly improved results, where are the super-voltage machines on the Continent? As far as I know there is only one million-volt unit, built during the last war, in Norway. Great therapy centres like Stockholm and Copenhagen did not have a single super-voltage unit at the end of 1953 and as far as I know still have none. At the end of 1953 a 400-KV unit had been installed in Stockholm. The 400-KV unit has no material advantage over a 250-KV unit. I am advised that there is not a super-voltage unit of the electrostatic or linear-accelerator type in Germany, France, Holland or elsewhere on the Continent. In Switzerland there is a 20-million-volt betatron, of which there are also 3 in Great Britain; they are very difficult to keep in satisfactory operation and they have not given worth-while results. There are also several betatrons in Germany. Incidentally, Tubiana *et al.*[5] did not get any results superior to those which may be obtained with conventional radiotherapy in the treatment of carcinoma of the oesophagus or carcinoma of the broncho-pulmonary system. Dr. Cohen poses the question, 'Is South Africa to be a unique exception?' One might just as well apply this question to Sweden, Denmark, Germany, France, Holland, and the rest of Europe, because there is not a single institute with megavolt therapy available apart from the betatrons in Switzerland and Germany. It is noted that even Dr. Cohen does not ask for a betatron.

Five years have elapsed since the 2-million-volt machines I referred to in my article[2] were installed in Great Britain and 20 years since the 1-million-volt machine was installed at Bart's. None of these is being replaced by similar machines. They are being replaced by linear accelerators of the 4-million, 8-million and 12-million-volt types. The 1-million and 2-million-volt machines must, therefore, have proved unsatisfactory or not have given worth-while results.

Even Blomfield,[6] of Sheffield, who has had a 2-million-volt machine since 1950 and whose article on the results has been published this year, cannot show any improvement in survival rates, although he claims the generally accepted advantages which have been known to us for many years, and which Dr. Cohen repeats.

If super-voltage therapy is so essential why is it that only a very small proportion of the hospitals in the British Isles are equipped with these machines when they have had the opportunity to observe them in operation for the last 20 years, and especially the last 5 years? In London at present, Bart's, the Postgraduate, the Westminster, the Mount Vernon and the Royal Marsden hospitals, are equipped with super-voltage machines. Why are Guy's, St. George's, St. Mary's, the London and the Royal Free hospitals not so equipped? Even the Middlesex Hospital, which has the Meyerstein Institute of Radiotherapy—one of the leading cancer therapy centres in Europe, directed by Professor Windeyer, who is a world-recognized authority on radiation therapy—is only now beginning to plan the installation of super-voltage apparatus as distinct from the Mount Vernon Hospital. (It is again recalled that the Middlesex Hospital has as many physicists as radiotherapists.) The Radium Institute, Liverpool, much larger than Johannesburg, and treating per annum about 400 new cases of cancer of the lung and 400 of the breast, has no super-voltage or large radio-active cobalt bombs yet. Must we apply the opinion to all these hospitals which are not equipped with super-voltage therapy that they are 'at variance with almost all enlightened opinion throughout the world'?

The latest book on radiotherapy, *British Practice in Radiotherapy*[7] (1955), edited by Sir Ernest Rock Carling, Professor B. W. Windeyer and Professor D. W. Smithers—the latter two being 2 of the 3 professors of radiotherapy in Great Britain and Ireland—which contains articles by the leading radiotherapists of Great Britain, has few references to super-voltage therapy merely stating that super-voltage therapy might have some advantage but by no means stating that it is essential. The Editors state (page 11), 'The progress of radiotherapy may well depend as much on the success with which it preserves some elasticity of organization and deliberately avoids its tendency to isolation as upon the construction of more powerful apparatus or the introduction of new treatment methods'. In the chapter on radiotherapy and X-rays Professor Windeyer, referring to the 200- and 250-KV machines and to their disadvantages, states: 'Machines in this range have, however, until recently been the most reliable and convenient in use and still remain the mainstay of the majority of X-ray departments'. He refers to the advantages of multi-million-volt units already mentioned and goes on to state that 'they are being used experimentally but so far they do not come into consideration in the established techniques of radiotherapy'.

Thus, while it is true that super-voltage therapy, *under suitable conditions with suitable staff*, makes the X-ray treatment less trying for the patient, it does not hold out any great promise of cures in regions where conventional therapy does not cure.

### *Palliative Therapy*

The main application of super-voltage therapy at present is in the field of palliative therapy. Here it plays its greatest role. I made the statement in 1948[10] at the South African Medical Congress, and there has been nothing published since then to alter the truth of this statement. The assertions by Dr. Cohen[1] that in deep-seated tumours a greater percentage of cures will be obtained with super-voltage therapy calls for some comment. Where are these deep-seated tumours which will be cured by radiation? In the chest? Blomfield,[6] who has operated the 2-million-volt unit as long as anybody in Great Britain, claims an improved survival rate of *one month* in carcinoma of the oesophagus with 2-million-volt therapy. He cannot claim any improvement in carcinoma of the lung, and in fact treats this with conventional radiotherapy.

Where else do we find these deep-seated tumours? In the abdominal cavity? No one has claimed any improvement in survival rate by radical super-voltage therapy in carcinoma of the stomach, the pancreas, the intestine, the kidneys, the bladder, the prostate, the ovaries or the uterus. These are surgical conditions and may require palliative radiotherapy. Blomfield claims better results in carcinoma of the cervix (but this is a combined form of treatment) and also in carcinoma of the bladder, but treatment of bladder carcinoma is generally of the intracavitary type with radium, radon or isotopes.

Dr. Cohen makes it appear that Dr. Paterson, one of the leading radiotherapists in Great Britain, who has both a linear accelerator and a betatron, advocates super-voltage therapy as a routine form of treatment. Those who have read Dr. Paterson's address[9] at the plenary session of the 1955 South African Medical Congress on *The role of Radiotherapy in the Treatment of Malignant Disease*, will know that, *except in connection with carcinoma of the bladder*, he does not mention super-voltage therapy, although he covers the whole field of malignant disease. This is what he says: 'X-ray therapy is for the later case and offers exceptional scope for what is now known as megavolt therapy—that is radiation in the million-volt ranges. Ordinary radical X-ray therapy at conventional deep-therapy levels remains, however, entirely practical and such megavoltage is not essential'. In fact, when a question was put to Dr. Paterson on the subject at one of his lectures, he mentioned that with super-voltage therapy they were getting many more rectal reactions than before. Again, discussing treatment of carcinoma of the cervix,[10] regarding the place of X-ray in combination with radium, he writes: 'Megavolt therapy in any form, including cobalt beam units, has been shown to be of great assistance in achieving this purpose elegantly, but is by no means essential'. Perhaps the best and most relevant point in all the papers read by Dr. Paterson at the 1955 Congress is the following: 'To get reliable results we are forced to provide not only a fairly high degree of specialized skill, but to back it when necessary with elaborate equipment and experienced lay staff, including the physicist'.[9]

Before closing this discussion on super-voltage apparatus, it would be appropriate to quote again from the 1953 presidential address to the Royal Society of Medicine, Radiological Section, by Dr. Constance Wood,[8] Director of the Radiotherapeutic

Research Unit, Medical Council, Hammersmith Hospital. She was the first in the field with an 8-million-volt linear accelerator and she has had vast experience of radium-bomb therapy. Referring to her researches, which took some 10 years, into the comparison of 200-KV wavelengths and wavelengths corresponding to 2 MeV, she states: (1) 'The results of this investigation did not show that the wavelengths of radiation *per se* within the limits of the experiment, i.e., 200KV and approximately 2 MeV, had any significant effect on clinical results.' (2) 'Although we can be sure, as I have already mentioned, that it will be possible to treat patients with a much greater degree of comfort, we have, I think, no reason to believe that there will be any spectacular improvement in cure rate by the use of technical advances inherent in super-voltage therapy.' (3) 'It seems reasonable to conclude that some factor in the tumour itself, a factor of which unhappily we are at present ignorant, has a far greater influence on the final prognosis than the particular form or technique of treatment employed.' (4) 'We may well doubt whether all the efforts which have gone into making great technical improvement in radiotherapy have yielded a commensurate return.' (5) 'The dream of the radiotherapist in former decades of obtaining an X-ray beam which would deliver a high dose to deep-seated tumours without damaging the skin has not been achieved. With this, however, has come the realization that improved techniques will not materially increase the cure rate of cancer.' Finally: (6) 'The dream of the radiotherapist today is that we may find ways of influencing the biological response of tissues to radiation and that it is in the realization of this hope that future progress in the next decade is most likely to be achieved.'

In what way do these opinions differ from the views I expressed in my article,[2] or as long ago as 1948 when I stated: 'Neither radiation nor surgery are the answer or likely to be the answer to cancer therapy. The oncologist of the future will be the biochemist'.[19] All this is obvious from the fact that no radiation from any super-voltage machine can cure a carcinoma of the stomach or a carcinoma of the colon. While it is true that super-voltage apparatus upsets the patient less than conventional radiotherapy, it can do a tremendous amount of harm when not given by a radiotherapist who is skilled and experienced with this type of apparatus. The radiotherapist should never run the risk of making the patient worse by his treatment if there is no reasonable hope of a cure.

### RADIOTHERAPY BOMBS

Referring to the recent Conference in Geneva on the Peaceful Applications of Atomic Energy, Dr. Cohen[1] writes: 'The widespread acceptance of telecurie units for routine radiotherapy, and their many advantages over conventional methods, was emphasized. Indeed, scores of such units have now been mass-produced, and are operating with gratifying success in the USA, the USSR, Canada, South America, Eastern and Western Europe, Australia, India, China and Britain'. I stated in my paper[2] that the first 1,000-curie bomb in Europe was installed at the Mount Vernon Hospital. It did not begin operating (and then only on a few selected cases) until April 1954. Another 1,000-curie bomb has been installed in Leeds, and a 2,000-curie bomb has been presented to Sir Stanford Cade but is not yet erected. There is probably only one other such unit in Europe, and that is in Italy. Dr. Cohen's statement alleges without any foundation that there are scores of such units all over the world, including Britain. (I mentioned that there were smaller units at various hospitals in Great Britain.) His reference is presumably to volume 10 of the *Peaceful Uses of Atomic Energy*,[11] where there are 3 papers on the subject of cobalt-60 teletherapy amongst 27 papers on isotopes.

None of these 3 papers discusses the results or compares them with conventional therapy. In the paper by Dr. Brucer,[12] Chairman of the Medical Division, Oak Ridge Institute of Nuclear Studies, U.S.A. a summary is published in table 4 of the cobalt-60 installations in the United States. It shows that out of 13 installations, there are only 4 of the 1,000-curie type. Neither of the 2 papers by Lanzy and Skaggs[13] on cobalt-60 therapy units or by Braestrup Monney[14] mentions results. Where does Dr. Cohen get his information about gratifying success in the countries he mentions throughout the world? His reference to running costs of the cobalt-60 sources completely omits the difficulties of transportation. To him the replacement of cobalt-60 does not offer any problems. On the other hand, to Dr. Brucer it is of considerable importance, because he states: 'The biggest problem in reloading teletherapy sources has been that of transportation of multi-ton containers'. I am advised that there are no facilities in England for replacing the cobalt in the 1,000-curie theratron. After a visit to Professor Mitchell at Cambridge in 1953, I attempted to get an iridium bomb, but after a great deal of correspondence it was found impossible because of transportation regulations and difficulties. What is the distance of Johannesburg from any reactor?

The biggest exaggeration is in Dr. Cohen's reference to caesium-137. He writes: 'In the near future cobalt-60 sources would be replaced by caesium-137, a by-product of uranium fission produced in embarrassingly large quantities by all atomic power plants, which will probably be given free to hospitals and industry to avoid expensive alternative methods of disposal.' He seems a little confused about the relative functions of the caesium and cobalt bombs. The authorities do not advise replacing cobalt bombs, which have an equivalent of about 2½ million volts, by caesium bombs, which have an equivalent wavelength of about 500,000 volts, but it has been suggested that the caesium bomb, which consequently requiries less protection, should replace the 250-KV radiotherapy unit, and this I understand is to be done at the Westminster Hospital with one of their X-ray units when caesium becomes available. There is little difference in the value of radiation at 500KV and 250KV. No caesium bomb is at present functioning in England.

What does Dr. Brucer have to say about it? He states: 'Probably the major disadvantage of caesium-137 has been the fact that it has not been available'.[12] He points out that there is only one caesium bomb, used as an experimental procedure, and that only two 750-curie pellets have been manufactured; and atomic piles have been operating in the USA for about 15 years.

Dr. Cohen would appear to be under the impression that gross fission products may be used for radiation purposes. Dr. Brucer states: 'Gross fission products are an expensive and uneconomical source of radiation. The caesium has to be separated from the gross fission products and this has caused many problems'. Far from being available in embarrassingly large quantities in the near future, a cable was received only a few days ago from Harwell stating that all caesium is booked for 2 years and that the cost of the caesium has not been determined by the authorities. Dr. Brucer[12] points out that the cost above 3 curies of caesium is unknown and that 3 curies costs 10,000 dollars, whereas 3 curies of cobalt-60 costs 600 dollars.

Dr. Cohen asks: 'Is South Africa to be a unique exception' in relation to the installation of cobalt units and super-voltage units? In my article[2] I stressed the difficulties of the shortage of personnel, both radiotherapists and physicists, and the dangers of running these units without them. They are not difficulties to Dr. Cohen. Referring to the supply of skilled physicists he says, 'South Africa is somewhat better off in this respect than most other countries, since the industrial demands have not yet developed greatly.' He adds: 'The successful construction and operation of the cyclotron . . . . by a locally-trained staff in Pretoria shows that this country does not lack physical skills'. The cyclotron took 4 years to build and it was directed by one physicist with constructional engineers, the senior of whom is now employed by private industry.

Professor Naude, head of the C.S.I.R., in his recent presidential address to the South African Association for the Advancement of Science, stressed the lack of skilled scientists. A senior physicist of the C.S.I.R. informed me this week that they were short of physicists. These facts are either unknown or ignored in the clamour for super-voltage therapy. I understand that Groote Schuur Hospital, Cape Town, has been unable to replace the physicist who left last year.

### AVAILABILITY AND QUALIFICATIONS OF PERSONNEL IN SOUTH AFRICA

I would also refer to the availability of radiotherapists. The standards laid down in 1950 by the Special Committee of the Canadian Cancer Association[15] for the head and deputy head of a department dealing with a population of 500,000 are as follows: (1) They must both be certified radiotherapists, (2) they must have at least 5 years' experience, and (3) they must have done tours of radiotherapy centres and departments in the USA, Canada and Europe. In Great Britain the directors and deputy directors of hospitals corresponding to the size of Johannesburg must have much more experience than 5 years and much higher qualifications than merely holding certificates or diplomas in radiotherapy. At about the time the Canadian committee was investigating the subject, Johannesburg appointed a radiotherapist conditionally

on his obtaining a diploma in radiotherapy and who did not at that time have the other qualifications necessary to be registered as a specialist radiologist. Only the Johannesburg Hospital Board of that time can give the reasons for the appointment. One can assume, however, that there were not many well-qualified applicants.

These were the conditions for routine radiotherapy in Johannesburg in 1949. Are they now better in relation to super-voltage therapy? Is there available a staff sufficiently skilled and experienced, clinically and radiotherapeutically, in the techniques required for the proper operation for a super-voltage unit or radioactive cobalt bomb of the 1,000-curie type?

### REGIONAL CENTRES

Dr. Cohen takes up some space, and not for the first time, with his views on the organization of a regional centre. He wrote on the subject in the *Journal*[3] of 11 December 1954, and in a letter on behalf of the Executive of the Radiological Society of South Africa Dr. H. Jackson[4] replied: 'The author's suggestions for the organization of the radiotherapy services in South Africa contain nothing new. They merely re-state incompletely the evidence given by the Transvaal Branch of the Radiological Society of South Africa in a memorandum submitted to the Gluckman Commission on 12 and 15 April 1943'. In this article of 11 December 1954 Dr. Cohen suggested that a 'radiologist' broadcasting on behalf of the Cancer Association advocated a district radiotherapy service staffed by part-time radiologists and financed by the Cancer Fund. He went on to state 'The danger of a multiplicity of smaller centres . . . . is exemplified by the following avoidable tragedies on record in our files', and also, 'The prospects of a multiplicity of rural units is an alarming one'.

Dr. Jackson[4] pointed out that there was no mention in the script of the broadcast of part-time radiologists, or of the establishment of multiple rural centres 'which is so alarming to the author of the article'. But here is the amazing point. In his latest article[1] Dr. Cohen advocates 'several peripheral clinics . . . . in populous suburban or rural areas, each having one inexpensive versatile medium-voltage therapy machine and one radiographer, with a radiotherapist sent from the centre for one or more weekly sessions to see new and follow-up cases and to prescribe treatment for those non-malignant conditions and simple palliative procedures which do not require the facilities and technical precision available at the larger hospitals'. This is completely contrary to what he had to say in December 1954.

Why is there this complete change of front between December 1954 and June 1956 on the subject of regional centres?

There is, one more very serious point which can no longer go unquestioned and unanswered.

### ALLEGATIONS ABOUT THE STANDARDS OF RADIOTHERAPY IN SOUTH AFRICA

Although quite irrelevant to the discussion on super-voltage therapy, Dr. Cohen persists in dragging the question of dosage into the discussion, as he did on the former occasion.[3] It is necessary, therefore, to take up certain allegations made by him. He states: 'Yet these advanced techniques have, apparently, no place in the type of radiotherapy which, with a few notable exceptions, is currently practised in this country, and which is generally characterized by systematic underdosage'. A reference to underdosage was made previously in the same terms.[3] He went even further at that time; thus, 'This malpractice' (underdosage) 'is excused by reasoning that cancer is incurable anyway and that all treatment is merely palliative, or that severe radiation reactions are "bad business" as they are considered undesirable by the referring physicians'. This is what Dr. Jackson had to say about it for the Executive of the Radiological Society: 'The Executive cannot condemn too strongly the derogatory statements made about the author's colleagues—both the clinicians on the staff of the Johannesburg General Hospital and elsewhere and radiologists. These statements accuse them of "malpractice" and being influenced by considerations of "bad business", merely because the author does not agree with their views on the dosage necessary under various conditions.'

What is the origin of these accusations? The following, apparently, is the explanation. On 15 April 1950 an article was published in the *Journal* by Dr. Cohen[21] on the *Scope of Irradiation of Cancer of the Breast*. After analysing the literature on the subject, he writes: 'An attempt will be made in this paper to elucidate the causes of failure in the therapy of mammary carcinoma by both surgery and radiation in view of the known pathology and radiobiology of this disease. It is hoped that the information will aid materially in designing more adequate radiotherapeutic techniques'. He goes on to say: 'Few of the standard techniques published by the world's radiotherapy centres solve the problems posed in the foregoing section'. So this radiotherapist, whose experience after taking his diploma must at that time have been limited, proceeded to tell the professors of radiotherapy throughout the world where they were wrong and what they should do.

This was his scheme of treatment: With conventional apparatus at 250KV and 5 fields as adopted by many radiotherapists, he proceeds to deliver the dose in 2 weeks, that is 10 treatments, shortened 'recently to a one-week technique'. The dose given is not less than 3,500 r to each field; thus each of the 5 fields receive 350 r daily for 10 treatments, so that a minimum dose of 3,500 r is given, in effect, in 12 days and a maximum of 4,000 r to the skin if exit doses are considered. This meant that *every day the patient received over the chest wall* 1,750 *r units*, a very large dose. Patients frequently complain of nausea after 600 r per day. Few will tolerate 800 r but here the women attending the Johannesburg General Hospital were submitted to 1,750 r units, with the result that 'a moist desquamation was obtained in all cases over all areas'.

Can one visualize what this moist reaction over half her chest, the supraclavicular region and the axilla, back and front, following a radical mastectomy, means to the patient in local pain and general disturbance? Where there is considerable prospect of curing a cancer with radiation, a vigorous reaction is justified, but there is no hope of curing any woman of her breast cancer by this treatment applied to the chest wall in 1-2 weeks. Only 20-25% of cases develop secondaries in the chest wall. The vast majority of patients (70-80%) who die from carcinoma of the breast do so from distant secondaries and not from recurrence in the chest wall. The most that one can hope for from this vigorous treatment is to stop some of the local recurrence in the 20-30% of cases who develop secondaries.

Dr. Cohen stated, 'Although several cases treated in this way have developed metastases, we had never seen a recurrence in the treated zone'. The use of the word 'never' after a few months' observation is to be noted. He does not mention the number of cases treated in the course of the year. Every student knows that to talk of 'never' after a few months' observation of cancer is wholly misleading. Moreover the cases were not graded or staged and even ages are not mentioned or any of the other factors which may influence the development of secondary deposits in the chest wall (Smithers *et al.*, 1952).[18] There is no mention of control cases.

Have there been any reports since 1950 of the results of this technique? Have the results been such that its continuation has been justified? Why was the technique abandoned? Yet Dr. Cohen alleges that it is only 'bad business' considerations which prevent other radiologists in other hospitals or private practice from adopting this technique. In his recent article[1] he says, 'These advanced techniques have, apparently, no place in the type of radiotherapy which, with a few notable exceptions, is currently practised in this country and which is generally characterised by systematic underdosage'. Who are the few notable exceptions? Where are the references to the radiotherapists or hospitals who deliver this dose in a week? The usual period of treatment is about 4-5 weeks, some radiotherapists going on for longer periods, sometimes to 10 weeks and more.[20]

The latest article on carcinoma of the breast (which only arrived two or three days ago) is by Professor Low-Beer[16] (Professor of Radiotherapy at the University of California, San Francisco). He gives 35 treatments, over 7 weeks, for a post-operative course of X-radiation in carcinoma of the breast. Professor Low-Beer, who unfortunately died recently, worked in one of the largest American hospitals at San Francisco. He also collaborated with the staff of the Donner Laboratories, at Berkeley, about half an hour away by car, where E. O. Lawrence (the inventor of the cyclotron) works with the largest cyclotron in the world at present, and where John Lawrence, the great isotope physician, also works. Professor Low-Beer, although he worked with the cyclotron, had not got any super-voltage radiotherapy or any large cobalt bombs.

So the whole world of radiologists—people like Baclesse[20] of Paris, Windeyer, Smithers, Paterson and so on in Great Britain,

and equally distinguished people in the United States—do not know how to treat breasts. These misguided therapists continue in their ignorance even after Dr. Cohen had published his method of treatment. But did Dr. Cohen himself believe in his technique and did his senior colleague at the Johannesburg General Hospital accept his discoveries?

If so, why was it changed? The *British Journal of Radiology* in December 1952 published an article on radiotherapy in breast cancer by Cohen and Shapiro.[17] Part 1 of the article is by Dr. L. Cohen; it deals with the dose—time relationship and theoretical considerations—and is mainly repetition. Dr. Cohen says that 'current cases are now treated with a standard technique'. (One assumes that this technique is the one he advocated in 1950.) He goes on to say: 'The optimal procedure seems to be the delivery of heavily filtered radiation homogeneously as possible to the whole of the potentially involved area within a relatively short period. In our experience 3,500 r tissue-dose delivered in 10 daily fractions meets these requirements and effectively prevents local recurrence'. One notes that the technique of giving the whole treatment in one week is not mentioned. Part 2 of the same article is by Dr. M. P. Shapiro, who advocates an entirely different technique for the treatment, particularly of post-operative cases, that is to say, the majority of breast cancer cases. One has but to compare the diagram given by Dr. Shapiro in 1952 and the diagram given by Dr. Cohen in 1950 to see the vast difference. Dr. Shapiro still uses high voltage to the sternal, inferior axillary, supra-clavicular and posterior axillary fields but, in the region where one may expect most secondaries to occur in the chest wall, he uses 3 fields with low voltage not cross-fired; yet Dr. Cohen advocated high voltage and cross-firing. The fields are quite different in size too. He uses 140KV with 2 mm. aluminium, and an applicator 20 x 7 cm. and 25 cm. F.S.D.—quite different from the factors given by Dr. Cohen. Although Dr. Shapiro also advocates a dose of 350 r, so that 3,500 r are given in 12 days, he only applies this to 3 fields and not the whole chest wall, so that the over-all time is 26 days, i.e. 5 weeks, and not 12 days or one week as Dr. Cohen advocated. Moreover, Dr. Shapiro states, 'We believe that high voltage X-ray therapy is not necessary for the treatment of the chest wall and that the described technique is more accurate than the usual employ of glancing fields', which Dr. Cohen advocated.

Here we have a technique advocated by Dr. Cohen in 1950 after indicating that the authorities throughout the world were wrong, and again advocated in the article in 1952, and rejected by his co-author and senior colleague at the Johannesburg General Hospital in the same article.

Dr. Cohen starts a technique without adequate control, starts an experiment and gives very large doses and causes marked reactions, because he thinks that is the correct answer to carcinoma of the breast. Nevertheless 2 years after the publication of the article the technique was apparently given up and a totally different technique adopted—not merely a minor variation—at what date we do not know.

Professor Berven, one of the leading radiotherapists in Europe, for many years at Stockholm, refused to change his technique for over 20 years because he stated (personal communication) that if he kept on changing and chopping his technique he would not know what technique was giving the best results.

What made Dr. Shapiro discard Dr. Cohen's technique? He states that this technique with low voltage to the chest wall is more accurate than Dr. Cohen's technique of glancing fields and high voltage to the chest wall.

A radiotherapist is entitled after reviewing the techniques of the world, to decide that he prefers this or that particular technique. Techniques vary a great deal. Some radiologists do not give any irradiation to the chest wall at all and some give an estimated dose of 4,000 r units, cross-fired, to the chest wall. Incidentally, Dr. Shapiro's technique also results in a moist desquamation over all fields.

We are not told in this combined article the reasons why Dr. Shapiro adopted this technique and discarded Dr. Cohen's, nor how soon after 1950 this change in technique was started and whether the technique has been changed again; yet it is from this quarter (Deep Therapy Department of the Johannesburg General Hospital) that unfounded accusations are made that all the other hospitals and private radiotherapists 'with a few notable exceptions' are guilty of malpractice. This is the only department which has been vociferously clamouring for super-voltage therapy and large radio-active bombs.

It may not have been worth discussing these allegations but for the fact that the position of Senior Radiotherapist at the Johannesburg General Hospital carries a considerable status. The holder of the post is automatically put on various committees, including the isotope screening committee, and is accepted as an authority. Radiologists, whether diagnostic or therapeutic, have claimed throughout the world that the status of the Radiologist in charge of the department should be equal to that of a senior physician or a senior surgeon.

It would be of interest to the profession to know what the results have been of the technique advocated by Dr. Cohen in 1950, why the technique was apparently changed in 1952, and whether it has been changed again since then. It would be of value to the profession to know whether the results have been good or whether undesirable effects have followed when the treatment has been given in 1-2 weeks. Telangiectasis, skin and rib necrosis requiring skin grafts, and pulmonary fibrosis, may have to be risked under certain conditions. It would be of value to the profession to know whether these techniques adopted or advocated have resulted in such changes occurring more frequently or less frequently than at other hospitals, in South Africa or abroad, where these techniques are not adopted. It is not only the techniques of X-ray therapy of the breast that should be investigated, but also the techniques employed in other conditions. How many patients, for instance, treated for spinal conditions have developed necrosis of the overlying soft tissues?

It is to be regretted, notwithstanding the opinion expressed on behalf of the Radiological Society on Dr. Cohen's accusations against his colleagues, that he should see fit to continue to make them with as little justification now as he had originally.

Super-voltage radiation and radio-active bombs undoubtedly have a place in radiotherapy and will play a large part in future at all therapy departments which are staffed by adequately-trained radiotherapists and physicists, but it must be apparent to all that the presence of such persons is a *sine qua non* for the proper use of these powerful machines.

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## MEDICAL PRACTITIONERS OF UNKNOWN ADDRESS

The Registrar of the South African Medical and Dental Council has supplied the subjoined list of medical practitioners (with their present registered addresses) to whom communications addressed by the Registrar have been returned by the Post Office because delivery could not be effected. Attempts to trace these practitioners have failed. Their attention is invited to the following sections of the Medical, Dental and Pharmacy Act:

Section 16 (2) It shall be the duty of every registered person who changes his address to intimate the fact to the registrar within one month after such change.

Section 17 (1) The Council may erase from the register the name of any person who . . . (b) has failed, within a period of three months from the date of an enquiry sent by the registrar by registered letter to the address appearing on the register in espect of him, to notify to the registrar his present address.

Hicksonia L. Cindi (neé Mahabane), 896 Dube Street, Tophelong, Vanderbijlpark.

H. T. P. Graf, General Hospital, Vereeniging.

Johannes Herzberg, 'St. Elmo', Lansdowne Road, Claremont, C.P.

D. M. King, Bedford, P.O. Klaserie, Transvaal.

H. L. Lello, 434 Manning Road, Durban.

J. G. Meidlinger, Blyvooruitsig Native Hospital, P.O. Box 1, Blyvooruitsig, Transvaal.

L. J. J. Muller, Union Health Department, P.O. Box 26, Cape Town.

H. A. Nel, Border Hotel, Prieska, K.P.

F. J. Preis, Athlone Hotel, Witbank.

N. S. Turnbull, 37 Belgravia Crescent, East london.

T. Weeks, Algemene Hospitaal, Johannesburg.

L. E. Whitfield, c/o J. Aitken, 17 Dieperink Street, Roodepoort.

## NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

*Collo-Cal-D Elixir:* The Crookes Laboratories Ltd., P.O. Box 1573, Johannesburg, write as follows:

The Crookes Laboratories Ltd., have introduced Collo-Cal-D Elixir with a higher Calcium and Vitamin D content than the standard preparation of Collo-Cal-D, giving a more potent and more palatable approach.

In producing an Elixir of Calcium with Vitamin D, the aim has been to provide a vehicle for Calcium and Vitamin D, which will not only remain stable and possess the right viscosity but be pleasant in flavour. Collo-Cal-D Elixir is a creamy orange-flavoured preparation that will be well tolerated by everyone. The Vitamin D potency has been increased to provide 500 i.u. Vitamin D3 to a teaspoonful and the Calcium content has been stepped up to provide 480 mg. in the same dose. Dosage depends on the need of the individual patient. Used prophylactically, 1-2 teaspoonfuls daily will be found adequate, but in cases requiring intensive theraphy 4-8 teaspoonfulls will be necessary. Packing 4 oz. bottle. The Crookes Laboratories Ltd,. P.O. Box 1573, Johannesburg.

## PASSING EVENTS : IN DIE VERBYGAAN

*Prof. L. H. Wells*, who succeeded Prof. M. R. Drennan as Professor of Anatomy in the University of Cape Town and assumed office in July 1956, was born in England and is now 47 years of age. He came to South Africa when he was 10 years old and went to school at St. John's College, Johannesburg. He proceeded to the University of the Witwatersrand, where he took the degree of B.Sc. in 1928, M.Sc. in 1930 and D.Sc. in 1946. He qualified M.B., B.Ch., in 1938. His theses for the mastership and doctorate in science were entitled 'The foot of the South African Native' and 'Muscular variation in the human leg and foot, with special reference to the South African Native'.

Prof. Wells

*photo; Cape Argus*

Dr. Wells held posts in the Department of Anatomy in the Witwatersrand University from 1932 to 1951, when he was appointed in the University of Edinburgh as Senior Lecturer in Physical Anthropology in the Department of Anatomy. In 1954 he became Reader of the latter department. In 1949 Dr. Wells was visiting lecturer in Physical Anthropology in the Anatomy Department of the University of Oxford.

Although Dr. Wells' work in physical anthropology has been widely noticed and has provoked much interest, a great part, probably the greater part, of his time has been spent on pure anatomy and the teaching of the subject to undergraduate and postgraduate students of medicine. He has published many articles, both anatomical and anthropological.

Dr. Wells is a Fellow of the Royal Society of South Africa and of the Royal Society of Edinburgh, and a Member of the South African Association for the Advancement of Science.

He is married and has a son and a daughter, both at school.

* * *

*Lecture by Dr. D. G. James.* Under the auspices of the Southern Transvaal Branch of the National General Practitioner's Group of the Medical Association of South Africa, Dr. D. G. James will lecture on 'Erythema Nodosum' on Monday 10 September at 8·15 p.m. in the Harveian Theatre, University of the Witwatersrand. All members of the Group and other medical practitioners are cordially invited to attend. Dr. James is visiting Johannesburg with his wife, Dr. Sheila Sherlock, of the British Postgraduate Medical School, who is in South Africa as a guest of the University of the Witwatersrand.

* * *

*Mothers' Clinics, Cape Town.* The South African Council for Maternal and Family Welfare have issued their report on the Cape Town Mothers' Clinics for the year 1955-56. Family planning is the main object of the work, and 206 clinic sessions were held during the year at 7 welfare centres of the Cape Town City Council and one of the Cape Divisional Council. The new cases numbered 1,002 (120 European and 882 non-European), the total attendances numbering 4,461. The average number of pregnancies per new case was 4·48.

* * *

1957 *Prize Essay Contest.* The American College of Chest Physicians offers 3 cash awards to be given annually for the best contributions prepared by undergraduate medical students on any

phase in the diagnosis and treatment of chest diseases (heart and or lungs). The awards have been increased for the 1957 contest: the first prize will be $500, the second prize $300, and the third prize $200. Each winner will also receive a certificate of merit. The winning contributions will be selected by a committee of chest specialists and will be announced at the 23rd Annual Meeting of the American College of Chest Physicians to be held in New York City, on 29 May to 2 June 1957. All manuscripts become the property of the American College of Chest Physicians. Applicants are requested to study the format of *Diseases of the Chest*, the official journal of the College, as to length, form, and arrangement of illustrations to guide them in the preparation of the essay. A copy of the journal will be sent upon request. The following conditions must be observed:

1. The completion of an application form, which may be obtained by writing to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, USA.
2. Five copies of the manuscript typewritten in English (double spaced) should be submitted at the above-mentioned address not later than 10 April 1957.
3. The only means of identification of the author shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside, enclosing the name and address of the author.

* * *

*Dr. Norman Klass*, M.B., D.Phys.Med., Specialist in Physical Medicine, of 1008 Cavendish Chambers, Jeppe Street, Johannesburg (telephone 22-8650) has taken over the Physical Medicine Specialist practice of the late Dr. H. Haden, of 65 Pasteur Chambers, Jeppe Street, Johannesburg.

* * *

*Dr. Reuben Sougin-Mibashan*, of Sea Point, has been admitted to the Membership of the Royal College of Physicians of London, and of Edinburgh. After qualifying at the University of Cape Town in 1949, he obtained his M.D. in 1954, with a thesis on 'Studies in Gout' Afterwards on a Nuffield Fellowship, he continued investigative work on anticoagulants and uric-acid metabolism at the Postgraduate Hospital, Hammersmith, London.

* * *

*Sir Charles Hastings, Charles Oliver Hawthorne and Katherine Bishop Harman Prizes*, 1957. The British Medical Association invite entries for these competitions. The essays (or whatever form the candidate desires his work to take) must reach the Secretary, B.M.A. House, Tavistock Square, London, W.C. 1, not later than 31 December 1956. The contribution, which must not have been published, must be unsigned, but must be accompanied by a note of the candidate's name and address. No limit of length is laid down, but 3,000-10,000 words would be suitable. A preliminary notice of entry is required, on an application form to be obtained from the Secretary, to whom also enquiries may be directed.

The Charles Hastings Clinical Prize of £75, and the Charles Oliver Hawthorne Prize of £50, which is the second prize, are for the promotion of systematic observation, research and record in general practice. Any member of the B.M.A. who is in general practice is eligible. Candidates are to confine their attention to their own observations in practice rather than to previously published work, though relative references should not be omitted. Contributions, which must not have been published, are to be typewritten or printed on one side of the paper only.

The Katherine Bishop Harman Prize of £75 is for the encouragement of research into disorders incident to pregnancy and childbearing. Any medical practitioners (*a*) in the British Commonwealth or the Republic of Ireland, and (*b*) any member of the B.M.A., wherever resident, is eligible. Competitors are free to select the work they wish to present, within the scope of the Prize. Contributions must be typewritten or printed in English.

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*Union Department of Health Bulletin.* Report for the 7 days ended 9 August 1956.

*Plague, Smallpox, Typhus Fever.* Nil.

## SOUTH AFRICAN ORTHOPAEDIC CONGRESS, DURBAN

The Fifth Annual Congress of the South African Orthopaedic Association was held in Durban on 13-17 August 1956. Amongst those contributing papers were Sir Walter Mercer, President of the Royal College of Surgeons of Edinburgh, Dr. Steele F. Stewart of Honolulu and Mr. F. C. Dwyer of Liverpool.

A symposium on tuberculosis was held in which the following papers were presented: The diagnosis and treatment of tuberculosis of the hip joint, Sir Walter Mercer, Edinburgh; Excision of the tuberculous hip, Dr. N. M. Thompson, Pietermaritzburg; Central dislocation arthrodesis in the radical treatment of tuberculosis of the hip joint, Mr. A. C. Boonzaaier, Johannesburg; Observations on local therapy in skeletal tuberculosis, Mr. C. J. Kaplan, Durban; Domiciliary treatment in orthopaedic tuberculosis, Mr. J. J. Commereli, Cape Town; Recent trends in the therapy of tuberculosis, Dr. H. G. Houghton, Durban.

A symposium on the 'Durban Mystery Disease', resembling Iceland Disease, was contributed by Mr. R. C. J. Hill and Mr. R. W. S. Cheetham, of Durban, and Mr. R. Percy-Lancaster of East London, to which Dr. G. D. English, Medical Officer of Health of Durban, also contributed.

The following papers were presented: Osteochondritis dissicans, Mr. R. Percy-Lancaster, East London; Recurrent sprains of the ankle-joint, Mr. J. F. P. Mullins, Durban; The treatment of flat feet in children, Mr. A. J. Helfet, Cape Town; The management of scoliosis, Mr. F. J. Hedden, Johannesburg; Malignant bone tumours, Dr. M. Findlay, Durban and Drs. P. D. de Villiers and D. Brink; Dysplasia of tendons of the feet as a cause of congenital deformities, Dr. Steele F. Stewart, Honolulu; Osteotomy of the os calcis in the treatment of pes cavus, Mr. F. C. Dwyer, Liverpool; Osteotomy of the os calcis for paralytic pes cavus, Mr. J. Craig, Johannesburg.

A visit was made to the Umlazi Hospital, where treatment of orthopaedic tuberculosis in the open air was demonstrated.

The Annual General Meeting of the South African Orthopaedic Association was held during the course of the Congress.

The social events included a cocktail party given by the Natal Branch of the Orthopaedic Association at the residence of Mr. and Mrs. R. C. J. Hill, 606 Essenwood Road, Durban; a public luncheon at Mayville Hotel; and a luncheon given by Messrs. Smith and Nephew at their factory in Pinetown, followed by a tour of the factory; a dinner-dance at the Hotel Edward; and the annual dinner of the South African Orthopaedic Association, which was held at the Durban Club on the evening of Wednesday, 15 August, when the guests of honour were Sir Walter Mercer, President of the Royal College of Surgeons of Edinburgh, and Mr. F. P. Fouché, F.R.C.S., Johannesburg, and other guests were Dr. Steele F. Stewart of Honolulu and Mr F. C. Dwyer of Liverpool.

## BOOK REVIEWS : BOEKRESENSIES

### OBSTETRICS

*A Manual of Practical Obstetrics*. Third Edition. By O'Donel Browne, edited and largely re-written by J. G. Gallagher. Pp. viii + 265 + 203 illustrations. 37s. 6d. net. Bristol: John Wright and Sons Ltd. 1956.

*Contents:* Part I. Pregnancy and its Complications. I. Pregnancy. II. Anatomy of the Birth Canal. III. Development of the Foetus and Changes in the Maternal System. IV. Antenatal Care. V. Complications of Pregnancy. Pseudocyesis. Signs of Parity. Part II. Normal Labour and Puerperium. VI. Normal Full-term Pregnancy. Preparations for Labour. Methods of Examination. VII. Course and Management of Normal Labour. VIII. Stimulants, Anaesthetics, and Analgesics in Labour. IX. The Normal Puerperium. Part III. Abnormalities in Labour with Natural Presentations. X. Abnormalities of the Third Stage.

XI. Occipito-posterior Positions. XII. Complications due to Uterine Abnormalities. XIII. The Forceps. XIV. Various Maternal and Foetal Complications. XV. Breech Presentation. XVI. Other Complications of Labour. Part IV. Haemorrhages of Pregnancy. XVII. Abortion. Molar and Tubal Pregnancy. XVIII. Miscarriage. XIX. Premature Labour, Partus Serotinus and Chorionepithelioma. XX. Ante-partum Haemorrhage. Part V. Toxaemias of Pregnancy. XXI. Eclampsism or Pre-eclampsia. Hyperemesis Gravidarum. Acute Yellow Atrophy of the Liver. XXII. Eclampsia. Part VI. Complications of Labour with Unnatural Presentations, and Abnormalities of Uterine Action. XXIII. Face, Brow, and Anterior and Posterior Fontanelle Presentations. Asynclitism. XXIV. Transverse, Oblique and Compound Presentations. XXV. Rupture of the Uterus. Secondary Uterine Inertia. XXVI. Prolapse and Presentation of the Cord. XXVII. Foetal Birth Injuries. Part VII. Abnormalities of the Puerperium. XXVIII. Puerperal Pyrexia. XXIX. Puerperal Sepsis. XXX. Pulmonary Embolism. Insanity during Pregnancy. Part VIII. Contracted Pelvis. XXXI. The Normal Female Pelvis. XXXII. Pelvimetry. Contracted Pelvis. Part IX. Induction of Labour. XXXIIII. Methods, Indications, and Technique of Induction. Part X. Obstetrical Operations. XXXIV. Version. XXXV. Pubiotomy and Symphysiotomy. XXXVI. Caesarean Section. XXXVII. Destructive Operations on the Foetus. Index.

The new edition of this Irish text-book has been prepared by Dr. J. G. Gallagher and reflects mainly the teaching at the National Maternity Hospital in Dublin. As the title indicates, the theme is essentially practical.

On the whole this is a sound text-book and one which should appeal to the undergraduate. There are however a few criticisms to be made. In discussing the conditions to be satisfied before applying forceps the author omits to say that the head in the pelvis should occupy a position favourable for delivery and that there should be a reasonable prospect of safe delivery. As an indication for forceps delivery most of us would regard 3½ hours in the second stage, even in a primigravida, as being rather too long a time to wait before interfering. One must strongly disagree with the statement that usually no anaesthetic is necessary in emptying the uterus in a case of incomplete abortion. As one may expect from a National Maternity Hospital text-book, a rather prominent place has been given to symphysiotomy, an operation which has very little appeal outside Dublin. The reviewer does not agree that 140 should be regarded as the upper limit of a normal foetal heart-rate—160 would be more acceptable.

The book is up to date, short and to the point, features which should find favour with the student who, however, should remember that some of the Dublin views expressed may not find general approval. The price of the book is somewhat high.

E.M.S.

NEUROSES

*The Neuroses in Clinical Practice*. By Henry P. Laughlin, M.D. Pp. xlii + 802. $12.50. Philadelphia and London: W. B. Saunders Company. 1956.

*Contents:* 1. The Nature and Origins of Anxiety. 2. The Anxiety Reactions. The Acute Anxiety Attack or Anxiety Panic, the Anxiety-Tension State, and Anxiety Neurosis. 3. Intrapsychic Mechanisms of Defense. 4. The Phobic Reactions. I. Fear and Its Avoidance. 5. The Phobic Reactions. II. The Phobias. 6. The Illusory Gains of Emotional Illness. 7. The Conversion Reactions. Somatic Conversion or Conversion Hysteria, and Physiologic Conversion. 8. The Dissociative Reactions. 9. Depression. 10. The Fatigue Reaction. Emotional Fatigue, The Fatigue State, and Neurasthenia. 11. Overconcern with Health. Hypochondriasis, Somatic and/or Physiologic Preoccupation. 12. The Obsessive-Compulsive Reactions. Part I. The Obsessive Character Defenses, The Obsessive Personality, and the Obsessive Type of Character Neurosis. 13. The Obsessive-Compulsive Reactions. Part II. The Obsessive-Compulsive Neuroses. 14. The Neuroses Following Trauma. Appendix: A Brief Outline Classification of Emotional and Mental Illness. A Glossary of Psychiatric Concepts and Terms. Index.

In spite of the fact that a vast amount has been written on the neuroses, it is extremely difficult to lay one's hands on a book from which one can gain an adequate understanding of these psychological disorders. Commonly, either the presentation of the subject is so over-simplified as to make it hopelessly uninstructive or, at the other extreme, one finds oneself floundering confusedly in a morass of psycho-analytical jargon. The author of the book under review has made a welcome compromise by producing a highly informative and at the same time readable treatise on the neuroses.

The book opens with the postulate that all psychogenic symptoms may be regarded as manifestations of, or responses to anxiety. This is followed by a description of the numerous unconscious mental mechanisms which are used to combat anxiety. The various types of neurotic reaction are then considered in turn, with the emphasis on the psychodynamics underlying the symptomatology. The reader's interest is held throughout as he follows the neurotic's pathetic battle against the constant threat of the de-repression—a most expressive term—of intolerable emotional conflicts. Numerous explanatory case-histories constitute a valuable contribution to the text.

Laughlin's approach to the neuroses is essentially a dynamic one and it is therefore not surprising to find that he treats his patients psychotherapeutically, and that he is sceptical of the value of drugs, shock therapies and hypnosis in the treatment of these cases.

This book is highly recommended to those who seek a better understanding of their neurotic patients and to those whose task it is to treat these unfortunate individuals.

H.C.

## CORRESPONDENCE : BRIEWERUBRIEK

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH

*To the Editor:* In the number of the *Journal* dated 28 July 1956 there is again a reference by a correspondent to alleged 'discount granted by the S.A.I.M.R'. Similar accusations have been made at Branch meetings and elsewhere during recent months. It appears to be necessary to clarify the position.

Some 20 years ago medical practitioners suggested to the Nursing Home concerned that it offer to collect all laboratory fees to save them the trouble of doing so and to stop the irritation of their being asked to meet laboratory fees for which they either received no payment at all or had to wait lengthy periods to recover. The Institute had no particular interest in initiating such a scheme but, as it met with the approval of the medical profession, agreed to the arrangement and allowed what was considered to be a reasonable discount against loss to the body accepting liability.

Since the advent after the War of a body of privately practising clinical pathologists in Johannesburg this procedure on the part of the Institute has been criticized at meetings of the Group. I therefore wrote reporting our procedure to the South African Medical and Dental Council, as I had repeatedly urged that the Institute does not wish to shelter behind the fact that it is a "body corporate".

At a Conference sponsored by the Medical Council regarding the 'Provision of Medical and Dental Services in Relation to Medical Ethics' held in Cape Town on 24 March 1956 the matter was raised by a representative of the Association. Since our procedure appeared to cause offence to at least some members of the Association I undertook to discontinue it. The necessary steps for implementing this undertaking were put in motion immediately on my return to Johannesburg.

Nevertheless the memorandum prepared by Dr. M. Shapiro *et al.* (in which the matter was mentioned) was submitted for publication, and appeared in the *Journal* on 12 May, nearly 2 months after the assurance had been given that the procedure objected to was being discontinued. It is unfortunate, to say the least, that not by a footnote or otherwise did the authors* indicate that their accusation no longer applied.

P.O. Box 1038
Johannesburg
8 August 1956

E. H. Cluver
*Director, S.A.I.M.R.*

* The authors are not responsible. The Memorandum was reported at the Federal Council meeting, which is why it was published with other Federal Council matters in the *Journal* of 12 May. We are sorry that being unaware of the decision of the S.A.I.M.R. to discontinue the procedure, the *Journal* did not publish the fact then. We are glad to do so now—Editor.